Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease

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COVID-19 Impact Statement

COVID-19 Impact Statement

This statement is provided for the aid and benefit of future readers to summarise the impact of the COVID-19 pandemic on the scope, methodology, and research activity associated with this thesis. The academic standards for a research degree awarded by City, University of London and for which this thesis is submitted remain the same regardless of this context.

1. Summary of how the research project, scope or methodology has been revised because of COVID-19 restrictions

Due to COVID-19 restrictions it was not possible to secure an equal number of participants within each age group. This has not impacted the outcome of the study.

2. Summary of how research activity and/or data collection was impacted because of COVID-19 restrictions, and how any initially planned activity would have fitted within the thesis narrative

Not unexpectedly, the COVID-19 pandemic had a large effect on many people's personal and professional lives. Due to lockdown in the Netherlands, schools were closed twice for a substantial period and we had to provide homeschooling to my young children. This took a lot of time and effort with inevitable slowing down of research progress. Furthermore, health problems of family members complicated the situation.

Work at the University of Applied Sciences in Utrecht (where I am employed as a full-time lecturer) also became challenging and required more time, as adjustments had to be made to the curriculum. On-line teaching required additional preparation time and students struggling with COVID-19 related problems needed much more help. As clinic coordinator for the university outpatient clinic, I had responsibility for the preventive COVID-19 protocol, including updates and compliance verification checks. As a result of these additional responsibilities the time that was originally allotted for research was greatly diminished.

3. Summary of actions or decisions taken to mitigate for the impact of data collection or research activity that was prevented by COVID-19

An extension was offered to partly compensate for the delay due to the COVID-19 pandemic. Additional MS Teams meetings were organized with my supervisors which made up for the lack of opportunity to visit the university during the pandemic.

4. Summary of how any planned work might have changed the thesis narrative, including new research questions that have arisen from adjusting the scope of the research project

I am pleased to report that in spite of all these challenges the objectives of the project remained unchanged.

Date of statement: 31/03/2022

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Declaration

I grant powers of discretion to the Department of Optometry and Visual Sciences, School of Health and Psychological Sciences, City, University of London to allow this project to be copied in whole or in part without further reference to me. This permission covers only single copies for study purposes, subject to the normal consideration of acknowledgement.

Abstract

The primary aim of this study was to establish age-related, normal limits of monocular and binocular spatial vision under photopic and high mesopic conditions. Photopic and mesopic Visual Acuity (VA) and Functional Contrast Sensitivity (FCS) were measured with both positive and negative contrast optotypes under both binocular and monocular viewing conditions using the Acuity-*Plus* (AP) test. The experiments were carried out in normally sighted participants, aged 10 to 86 years. Data from participants who failed to meet pre-defined normal sight criteria were not included in the analysis. Mean and ±2.5σ were calculated for participants within 5-year subgroups. A biologically meaningful model was then fitted to these data. The Gauss-Newton method was used to calculate optimum, best-fit model parameters to predict mean values and upper and lower threshold limits for VA and FCS. These limits describe the effects of normal ageing on spatial vision for each of the 16 experimental conditions investigated. Out of the 382 participants recruited for this study, 285 participants passed the selection criteria for normal aging. Log transforms were applied to ensure approximate normal distributions. Outliers were also removed for each of the 16 stimulus conditions investigated based on the ±2.5σ limits criterion. The results show that under photopic conditions, the overall variability in results for both VA and FCS remained age-invariant up to ~50 years. A lower, age-invariant limit of ~ 30 years was more appropriate for the mesopic range with a gradual, but accelerating increase in both mean thresholds and inter-subject variability above this age. Binocular thresholds were smaller and much less variable when compared to either eye. This study has established upper normal, age limits for monocular and binocular viewing under photopic and high mesopic lighting conditions with both positive and negative contrast optotypes using a single test which can be implemented either in the clinic or in an occupational setting. Measurements of participants excluded from analysis due to systemic and/or ocular conditions were analysed separately and plotted against the newly established age-related normal limits of spatial vision in both lighting conditions. A substantial number of those excluded failed to meet the age-related normal limits established in the study. These preliminary findings suggest that the new age-related normal limits may turn out to be very useful in screening for systemic and ocular conditions in clinical practice.

List of Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
AMD	Age-Related Macular Degeneration
AP	Acuity-*Plus*
BCVA	Best Corrected Visual Acuity
CAD	Colour Assessment and Diagnosis test
cd/m^2	Candela per square meter
CI	Confidence Intervals
CIE	Commission Internationale de l'Elcairage
CPD	Cycle per degree
CRT	Cathode Ray Tube
CS	Contrast Sensitivity
CSF	Contrast Sensitivity Function
CT	Contrast Threshold
CTs	Contrast Thresholds
ETDRS	Early Treatment Diabetic Retinopathy Study
Exp	Exponential
FACT	Functional Acuity Contrast Test
FCS	Functional Contrast Sensitivity
FrACT	Freiburg Visual Acuity and Contrast Test
HDL	High Density Lipoprotein
HVFA	Humphrey Visual Field Analyser
LASEK	Laser Assisted Subepithelial Keratectomy
LASIK	Laser Assisted In Situ Keratomileusis
Lb	Luminance Background
LCD	Liquid Crystal Display
LE	Left Eye
LNL	Lower Normal Limit
Lo	Luminance Optotype
LoAs	Limits of Agreements
LOCS	Lens Opacities Classification System
log	Logarithm
logMAR	Logarithm of the Minimum Angle of Resolution
Lt	Luminance Target
M	Mean

m	Meter
MOA	Minutes of Arc
MPOD	Macular Pigment Optical Density
ms	Milliseconds
n	Number
ND	Neural Density
OCT	Optical Coherence Tomography
PCT	Percentage
PRK	Photo Refractive Keratectomy
RE	Right Eye
s	Seconds
SD	Standard deviation
Trans PRK	Transepithelial Photo Refractive Keratectomy
UNL	Upper Normal Limit
VA	Visual Acuity
VF	Visual Field

1. Introduction

1.1 Background

Visual Acuity (VA) measurements quantify the ability to resolve fine spatial detail and are one of the most common procedures in clinical practice (Wai et al., 2021). The majority of VA tests performed in clinical practice employ photopic lighting conditions and high contrast optotypes. Despite the fact that these tests are easy to perform and generally useful, they are not a good representation of working environments. In addition, high contrast VA tests have poor sensitivity in detecting small changes in spatial vision in the earliest stages of ocular disease (Lupión Durán et al., 2021; Klein et al., 1995; Pondorfer et al., 2020; Puell et al., 2012). Additional measurements of VA in mesopic conditions may overcome some of these limitations (Wood and Owens, 2005). In addition to VA, contrast sensitivity (CS), defined as the reciprocal of stimulus contrast at a threshold, also yields useful information on the kind of spatial vision one can achieve. Contrast is the fractional change in target luminance with reference to the background luminance (*Lt* = Luminance target*, Lb*= Luminance background*)*:

$$Contrast = \frac{Lt}{Lb} - 1$$

Contrast sensitivity function (CSF) relates contrast sensitivity to sinusoidal grating spatial frequency. Compared with VA, CS is a better predictor of visual performance in normal daily tasks (Freeman et al., 2006; Owsley and McGwin, 2010; West et al., 2002). However, studies like these should be treated with caution. Various aspects of visual functioning are of importance; the function of the eye, how the person functions and quality of life (Colenbrander, 2010). VA and functional contrast sensitivity (FCS) are examples of visual function parameters, functional vision describes task performance such as reading and quality of life indicates the impact of vision at a social level. The measurement of functional vision results in more relevant performance measures of activities of daily living, but is more complex and time consuming to measure (Colenbrander, 2010). Therefore, in clinical practice measurements are often limited to visual function measurements. Each of these aspects requires different assessments, and it is important to be aware of these different aspects. When utilizing questionnaires it is useful to evaluate the three different aspects separately (Colenbrander, 2010). FCS has also been shown to be

more sensitive to changes in image quality caused by the optics of the eye. Decrease in VA and FCS can also be attributed to neural changes with increasing age caused by reduction in cone sensitivities and loss of photoreceptors (Werner and Steele, 1988), reduced photon absorption efficiency in cones (Silvestre, Arleo and Allard, 2019), and/or neural changes in the retina by normal ageing and/or disease (Wai et al., 2021; Maynard, Zele and Feigl, 2016; Bittner and Ferraz, 2020; Midena et al., 1997; Müller et al., 2019; Gillespie-Gallery et al., 2013; Roh et al., 2018; Kleiner et al., 1988; Feigl et al., 2011). It is also of interest to perform contrast sensitivity under mesopic light levels. Loss of sensitivity with decreasing retinal illuminance is an indicator of age-related changes and/or the presence of early-stage ocular disease (Gillespie-Gallery et al., 2013). Other important reasons to test spatial vision under mesopic conditions relate to changes in pupil size. Higher order aberrations and retinal illuminance are affected by pupil size and can also alter the effect of scattered light (Patterson, Bargary and Barbur, 2015). A decrease in photopic VA and FCS beyond ~60 years of age was found as a result of normal ageing (Sjöstrand et al., 2011; Elliott, Yang and Whitaker, 1995; Haegerstrom-Portnoy, Schneck and Brabyn, 1999) and in mesopic conditions the decline starts at an earlier age (Puell et al., 2004b; Mäntyjärvi and Laitinen, 2001; Maynard, Zele and Feigl, 2016). It is well known that density of the rod photoreceptors declines with age (Curcio et al., 1993). Retinal ganglion cell loss and/or damage to their retinal axons can also contribute to the worsening of VA and FCS in normal ageing (Calkins, 2013). It is well documented that FCS is more sensitive in the early detection of retinal disease in comparison with VA, in both, photopic and mesopic light conditions (Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Martínez-Roda et al., 2016). Normal VA and FCS age limits for both light conditions may make it possible to separate normal age changes from those caused by disease. These normal limits are also of benefit in the vision screening carried out both in occupational environments as well as in the clinic. The Acuity-*Plus* test supports VA and FCS measurements in both, photopic and mesopic light conditions, using standard protocols. The standard protocol and interleaved measurements of four parameters with one single test result in the same test conditions, for example optotype and presentation duration. In addition to the most commonly used negative contrast optotypes, VA and FCS thresholds are also established with positive contrast. The combined assessment of VA and FCS using photopic and mesopic light levels with optotypes of positive and negative contrast provides a better description of the participant's spatial vision. Brief stimulus presentation time is part of the standard protocol and offers significant advantages. Multiple fixations are eliminated and the

test becomes more sensitive for both VA and FCS, particularly in patients with retinal disease who may also experience poorer temporal responses (Heinrich, Kruger and Bach, 2010). This study determines age-related normal monocular and binocular limits of spatial vision. These limits were obtained for photopic and mesopic conditions, and in negative and positive contrast polarities. The established limits may benefit the assessment of spatial vision in clinical practice, occupational health and in clinical research.

1.2 Synopsis

Chapter 1: The background, synopsis and aim of the project are given.

Chapter 2: History and general introduction to measurements of VA are described. The measurements of photopic and mesopic VA measurements are outlined. Existing literature about the effect of healthy ageing on photopic and mesopic VA is reviewed.

Chapter 3: This chapter starts with a general introduction of FCS measurement. The measurements of photopic and mesopic contrast sensitivity are examined in the literature. The effect of normal ageing on photopic and mesopic FCS is described.

Chapter 4: The material and methods of the primary aim of the study are described. The participant recruitment and ethical considerations are outlined in detail. The primary aim is to establish age-related normal VA and FCS thresholds with the Acuity-*Plus* test using a standardized protocol. The Acuity-*Plus* test is described in detail, as well as the complete history taking and full eye examination performed in all participants. The strict selection criteria to include only participants with normal photopic and normal mesopic vision are documented in successive steps.

Chapter 5: The effect of the novel method to filter participants who do not fulfil the criteria for normal photopic vision and normal mesopic vision is described. The effect of normal healthy ageing on photopic and mesopic VA and FCS thresholds in both light conditions and contrast polarities were established. Normal age-related VA and FCS limits were obtained for photopic and mesopic conditions. These limits were determined under monocular and binocular viewing using both positive and negative contrast optotypes producing best fit, non-linear, Gauss-Newton models.

Differences between negative and positive contrast, sex, right and left eye and testing sites were examined for VA and FCS thresholds.

Chapter 6: The results of the effect of healthy ageing on VA and FCS thresholds, and the established age-related normal limits are discussed. Strengths and limitations of the study are described. Valuable applications of the normal age-related limits are discussed and the conclusion of the study summarised. Recommendations for further research are given.

Chapter 7: In this highly exploratory study the application of the established age-related normal VA and FCS limits were examined. The results of participants with systemic disease that may affect the eye and ocular conditions were plotted against the normal limits. The results in this study were discussed and conclusions are given. Further recommendations are provided with regard to future research.

Appendices: Appendix A reports results on experiments designed to assess the inherent, within-subject variability in VA and FCS tests carried out in this study. These included monocular and binocular VA and FCS tests for each of the two lighting conditions and stimulus contrast polarities. The remaining appendices show the information sheets and informed consent sheets used at the different testing sites in addition to conference abstracts.

1.3 Aims of the Project

The aims of the study were:

1. To establish age-related normal limits of monocular and binocular spatial vision under photopic and mesopic conditions. In normally sighted participants photopic and mesopic VA and FCS thresholds using both negative and positive contrast optotypes under monocular and binocular viewing will be measured using the Acuity-*Plus* test. Gauss-Newton models will be used to calculate the normal limits for each specific age.

2. Highly exploratory study to investigate the application of established age-related normal VA and FCS limits. In this study the VA and FCS results of participants with systemic disease which can affect the eye and ocular conditions will be plotted against age-related normal limits.

3. To investigate the repeatability of all the VA and FCS measurements in photopic and mesopic conditions with the Acuity-*Plus* test. This Includes measurements using negative and positive contrast and under monocular and binocular viewing.

2. Visual Acuity

2.1 Introduction to Visual Acuity

Clinical assessment of VA is essential in routine eye examinations in optometric and ophthalmology practice and is usually tested at 100% contrast (high contrast) (Kniestedt and Stamper, 2003). Most patients visiting an optometrist or ophthalmologist will receive an eye examination, including determination of VA. VA measurements are used to dispense the most optimal prescription of glasses or contact lenses and evaluate ocular diseases. These measurements are also used to assess suitability for driving motor vehicles and for many occupational standards such as pilots and firefighters (Chisholm et al., 2003; Gruber et al., 2013; Kimlin, Black and Wood, 2017; Rubin et al., 2007).
Assessing VA is also essential in clinical trials and is often one of the primary outcome measures (Beck et al., 2007).

2.2 The measurement of Visual Acuity

VA has a long history, with the first tests of VA being recorded more than 5000 years ago by the Egyptians (Levin et al., 2011). VA is defined as the limit of spatial vision and in the past four different definitions of VA were accepted; minimum visible acuity, which is the smallest object that an individual can see, minimum resolvable acuity, which is the ability to distinguish between neighbouring objects, minimum recognizable acuity, which refers to the angular size of the smallest character that one can identify and minimum discriminable acuity, which is the angular size of the smallest change one can recognize (Levin et al., 2011). Minimum recognizable acuity is the standard method used in daily practice, and the letter charts of Donders and Snellen (figure 2.1 A), first introduced at the Eye Hospital in Utrecht, Netherlands, in 1862 are well known. Despite the popularity of VA measurements, it is not a very good indicator for vision in general and has several shortcomings. It can fail to detect small changes in early stages of ocular disease such as diabetic retinopathy, glaucoma and age-related macular degeneration (Puell et al., 2012; Pondorfer et al., 2020; Lupión Durán et al., 2021; Klein et al., 1995). In glaucoma for example, visual field loss will precede VA loss. Some of these shortcomings may be overcome by also measuring VA at a lower light level in the high mesopic range (Wood and Owens, 2005).

Anatomical and physiological factors can limit VA as can uncorrected refractive errors, higher-order aberrations, diffraction and scattered light (Levin et al., 2011). In clinical practice, VA is usually measured with negative contrast optotypes on illuminated test charts, i.e. black optotypes produced by depositing spectrally neutral pigments on a high reflectance, neutral background. Although differences in spatial vision between negative and positive contrast have been examined in previous studies (Alexander, Xie and Derlacki, 1993), little has been done to produce standard methods for assessing spatial vision with both contrast polarities. Although negative contrast optotypes do not always yield lower contrast thresholds, the majority of studies report better performance with negative contrast stimuli (Piepenbrock et al., 2013; Hwang and Peli, 2016), both in terms of VA and FCS as well as absolute detection thresholds when measured with decrements in luminance.(Blackwell, 1946). When used in the clinic in patients with early stage retinal disease and high levels of scattered light, contrast polarity may produce unexpected results with lower thresholds corresponding to positive contrast optotypes (González et al., 2007; Westheimer et al., 2003). Such findings reveal the importance of establishing upper normal age limits of spatial vision using optotypes with both positive and negative contrast with applications in visually-demanding occupations as well as in the clinic. Another parameter that affects the outcome of VA tests, particularly in patients with loss of spatial vision as a result of early retinal disease, is the stimulus presentation time. Normal ageing affects the temporal impulse response function of the eye with significant loss of the inhibitory phase of the impulse response in some older individuals and the subsequent loss of temporal sharpness and reduced response amplitude (Shinomori and Werner, 2003). Although the stimulus presentation time can affect the outcome of VA tests in normal individuals at very short stimulus durations (Heinrich, Kruger and Bach, 2010), the effect is much larger when spatial vision is assessed in patients with age-related macular degeneration who are less able to process briefly presented stimuli. Such patients require much longer times to achieve best acuity compared to age-matched, healthy individuals (Kono and Yamade, 1996). Longer presentation times also result in multiple fixations and this can aid the self-selection of the least-affected retinal area that yields the highest sensitivity. The use of briefly presented optotypes in VA tests to eliminate multiple fixations is more likely to reveal spatially localized damage on the retina and poorer temporal responses that can also be attributed to early stage retinal disease. Less common is the use of grating acuity, for example the Teller Acuity Cards (McDonald et al., 1985). These cards are designed to measure the highest spatial frequency an observer can resolve. Black

and white gratings are printed on one half of the cards, and the spatial frequencies increase across the cards. The looking behavior or pointing out the gratings determine the VA of the participant. These tests are useful in pediatric optometry, in patients with learning disabilities and in dementia (Friedman et al., 2002).

2.3 Photopic Visual Acuity

Photopic VA measurement is the most common routine procedure in clinical practice or preclinical research and determines the patient's ability to resolve fine detail in high contrast (Kniestedt and Stamper, 2003). Photopic VA is also described with the term standard VA; the first description is used in this study. Photopic VA is a crucial clinical parameter to establish best-corrected visual acuity (BCVA), check progression in ocular disease, in clinical trials, screening in specific occupational settings, and determination of requirements to obtain a specific certificate, for example a driving license (Rubin et al., 2007; Chisholm et al., 2003; Beck et al., 2007).

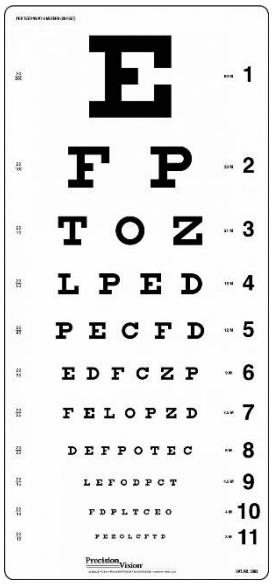
High contrast VA is the most common form of VA test and identifies letters or symbols of decreasing size. The most common VA tests employ high light levels when the pupil size and higher order aberrations are small and retinal sensitivity to contrast is high. The results of the tests are often not representative of typical working environments, but are easy and simple to carry out and in general extremely useful. VA tests are not, however, sufficiently sensitive to measure changes in visual performance caused by increased higher-order aberrations and scattered light (Applegate et al., 2003).

There are a variety of charts and optotypes used to measure VA (Kniestedt and Stamper, 2003). The charts with letters, E's and Landolt C are well known. In clinical practice, different formats are used, projected, printed and computer-generated. A commonly used printed chart is the Snellen chart (figure 2.1 A), developed by the Dutch ophthalmologist Herman Snellen. The number of optotypes (letters or numbers) on the Snellen chart increases on each subsequent line with different inter-letter spacing. The change in letter size between subsequent lines is also different, and therefore the accuracy level strongly depends on the acuity level (Levin et al., 2011). For example, the change in letter size between 6/60 to 6/36 is larger than the change in letter size between 6/18 and 6/12. The Bailey-Lovie chart (figure 2.1 B) developed by Bailey and Lovie (Bailey and Lovie, 1976) conversely uses the same number of letters on each line and proportional spacing between letters. Nowadays, most charts incorporate this design. Their V shaped appearance

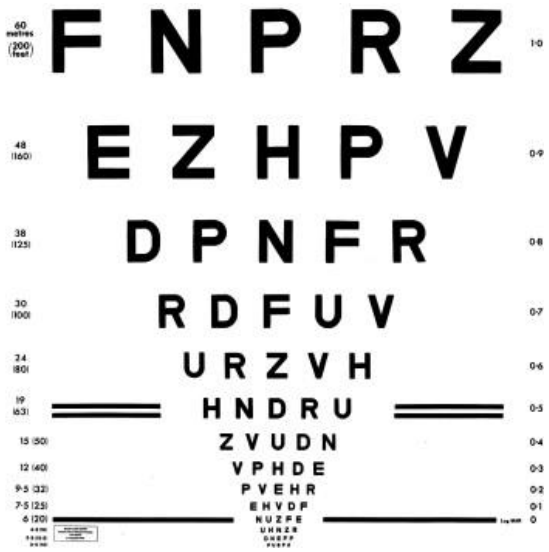
makes these charts easily recognisable as each line is smaller than the preceding line. The Early Treatment of Diabetic Retinopathy Study (ETDRS; figure 2.1 C) charts use the same principle, and were developed for use in the Early Treatment Diabetic Retinopathy Study (Ferris et al., 1982). There are however some differences between the Bailey-Lovie and ETDRS chart. The standard testing distance is 6 m with the Bailey-Lovie chart and 4 m with the ETDRS chart. Furthermore, the letters used with the Bailey-Lovie and ETDRs charts are British Standard letters and Sloan letters respectively (Bailey and Lovie-Kitchin, 2013). In figure 2.1 (A-C) the Snellen, Bailey-Lovie and ETDRS charts are shown.

In contrast with Snellen charts, the differences between each subsequent row in logMAR charts is 0.10 log units, and each row contains five letters. Therefore, it is possible to score for every letter read successfully. Each letter read successfully corresponds to an equal value (0.02 log units). Letter-by-letter scoring results in a more precise VA determination in comparison with row-by-row scoring (Bailey and Lovie-Kitchin, 2013).

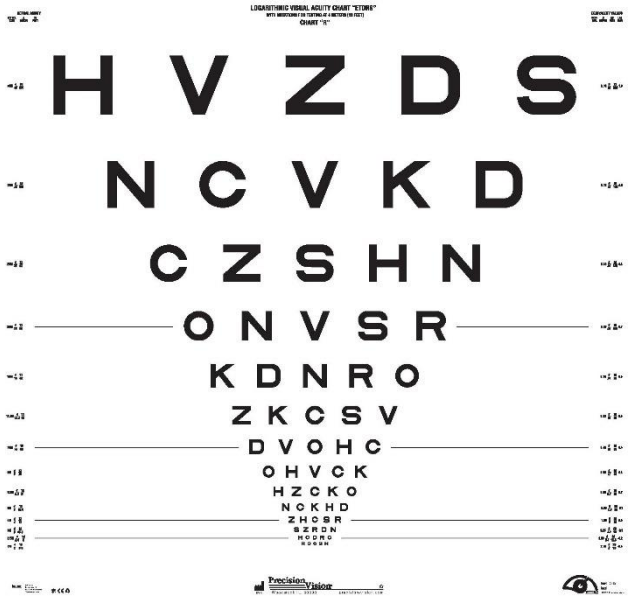
There is an increasing trend to use computer-based displays in VA assessment, particularly since the onset of the COVID-19 pandemic as these types of presentations also lend themselves well to use at home (Claessens et al., 2021). For research purposes, a computerized version of the ETDRS was developed; the E-ETDRS chart. The E-ETDRS version results were in good agreement with the conventional ETDRS chart (Beck et al., 2003). However, the E-ETDRS chart presents single Sloane letters surrounded by four bars, which is different to reading letters in a row. The use of computerized VA tests has some advantages in comparison to conventional or projector charts. Computerized charts allow different optotypes, spacing distance, colour, luminance level, presentation time and methods to determine maximum thresholds (Bailey and Lovie-Kitchin, 2013). Changing these parameters will directly affect the VA results. Development of computer generated tests also results in challenges, such as display resolution, dealing with unexpected responses of the patient such as pressing the wrong response button, stability of acuity measures and accurate determination of threshold (Bach, 2007). Most VA tests used in clinical practice are based on continuous viewing, for example, the ETDRS and Snellen charts. However, the use of VA tests with limited presentation duration influences the results of VA measurement (Heinrich, Kruger and Bach, 2010; Adrian, 2003). Normal ageing affects the temporal impulse response function of the eye with significant loss of the inhibitory phase of the impulse response in some older individuals and the subsequent loss of temporal sharpness and reduced response (Shinomori and Werner, 2003).



(A)



(B)



(C)

Figure 2.1 (A-C) The Snellen (image courtesy of Precision Vision) (A), Bailey-Lovie (Bailey and Lovie-Kitchin, 2013) (B) and Early Treatment of Diabetic Retinopathy Study (ETDRS) (image courtesy of Precision Vision) (C) visual acuity charts.

Heinrich et al. (Heinrich, Kruger and Bach, 2010) used the Freiburg Visual Acuity Test (FrACT) with different presentation times, including 10, 1 and 0.10 s. The FrACT is a computer-generated test that presents Landolt C rings on an LCD screen. The single stimuli were presented monocularly, and participants were asked to make a judgment about the location of the gap in the Landolt C. They found improved VA with longer presentation times of the optotype and the difference was more pronounced between 0.10 and 1 second.

Test illuminance is also essential in determining maximum VA thresholds (Johnson and Casson, 1995; Sheedy, Bailey and Raasch, 1984). The results of a study with different photopic luminance levels (40-600 cd/m²) showed a significant improvement of VA thresholds with increasing luminance levels (Sheedy, Bailey and Raasch, 1984). In clinical practice, both VA and FCS are measured with negative contrast optotypes on illuminated test charts, i.e. black optotypes produced by depositing spectrally neutral pigments on a high reflectance, neutral background. Previous studies have examined the differences in spatial vision between negative and positive contrast (Alexander, Xie and Derlacki, 1993), but little has been done to produce standard methods for assessing spatial vision with both contrast polarities. Although negative contrast optotypes do not always yield lower contrast thresholds, a majority of studies report better performance with negative contrast stimuli (Piepenbrock et al., 2013; Hwang and Peli, 2016), both in terms of VA and FCS as well as absolute detection thresholds when measured with decrements in luminance (Blackwell, 1946). When used in the clinic in patients with early stage retinal disease, contrast polarity may produce unexpected results with lower thresholds corresponding to positive contrast optotypes (González et al., 2007; Westheimer et al., 2003). Such findings reveal the importance of establishing upper normal age limits of spatial vision using optotypes with both positive and negative contrast for use in occupational health as well as in the clinic. Other patient related factors affecting VA are pupil size, refractive error and the area of the retina stimulated (Kniestedt and Stamper, 2003). Depth of focus for example depends to a great extent of pupil size, smaller pupils increase depth of focus (Labhishetty et al., 2021). The testing distance can also yield reduced VA results, particularly in presbyopic individuals when testing distance is close and exertion of accommodation is required (Green, Powers and Banks, 1980; Smith, 2006).
As a result of differences in parameters, VA thresholds of various tests are difficult to compare (Koenig et al., 2014; Kaiser, 2009; Kuo et al., 2011; Tiraset et al., 2021; Plainis et al., 2013). It is desirable to standardize photopic VA measurement, preferably using a method that is comparable with other measurements such as FCS and low light level performance.

2.4 Mesopic Visual Acuity

The measurement of photopic VA is routinely carried out in clinical practice, despite not being particularly sensitive to early-stage disease or valuable in differentiating between different stages of retinal disease (Rubin et al., 2001; Pondorfer et al.,

2020). Mesopic VA is rarely measured in clinical practice and primarily performed in research circumstances. The lack of availability of mesopic VA tests in most clinical practices, and no standardized protocols may be the reason. It is well known that VA decreases under lower light levels (Rabin, 1994; Sheedy, Bailey and Raasch, 1984; Johnson and Casson, 1995). Mesopic VA and Low Luminance VA (LLVA) are both terms used to describe VA in low light levels. In this study, the description mesopic VA is used. Another frequently reported term is the low luminance deficit (LLD) which is the difference between photopic VA and mesopic VA. Mesopic conditions involve light intensities equivalent to standard indoor lighting, street lighting scenarios and moonlight, encompassing the range from 0.01 to 10 cd/m² (Schwartz, 2010; Wood et al., 2021). It has been reported that VA remains stable between 100 and 1 cd/m², however changes were significant below luminance levels of 1 cd/m² (Rabin, 1994). Nevertheless, assessment of spatial vision in the high mesopic range remains important, largely because many working environments that require adequate spatial vision, often involve lighting levels in the high mesopic range (Li et al., 2020; Wood, 2020). Normal visual performance in the mesopic range is also important in safety-critical occupational environments involving pilots, air traffic controllers, train drivers, seafarers, rapid response drivers, fire arms officers and fire fighters. For example, in the Salisbury Eye Evaluation Study, luminance levels of 5.2 cd/m² were used to investigate whether mesopic VA is a predictor for car crash involvement (Rubin et al., 2007). A luminance level of 5.2 cd/m^2, although considered low in this study, is higher than the working luminance levels encountered in a number of occupations. Many environments, including lighting in residential streets and some occupations, employ lower light levels that fall in the upper mesopic range (i.e., 0.35 to 5 cd/m²) (Li et al., 2020; Wood, 2020; Rubin et al., 2007). Mesopic high contrast VA is therefore a better predictor of night time driving performance than photopic high contrast VA (Kimlin, Black and Wood, 2017; Gruber et al., 2013). Useful clinical information can often be obtained at lower light levels and the ability to maintain good spatial vision in the mesopic range has been taken as an indicator of the health of the retina (Gillespie-Gallery et al., 2013). It is therefore generally agreed that the assessment of VA should not be limited to only photopic conditions, but should also be measured at lower light levels when poorer performance can be indicative of impaired photon absorption efficiency in photoreceptors (Silvestre, Arleo and Allard, 2019), and/or neural changes that precede retinal disease (Owsley et al., 2016a).

Despite the obvious advantages of testing VA in the mesopic range, standard methods have not been developed and upper normal limits of spatial vision in the

mesopic range have not been established (Wood and Owens, 2005; Wood et al., 2021; Lin, Ng and Nguyen, 2015). This makes screening for abnormal responses and the comparison of results from different studies difficult to carry out. Different approaches are used to determine mesopic VA; reduced background luminance level, the use of neutral density filters, or a combination of both (Wood et al., 2021; Lin, Ng and Nguyen, 2015). Neutral density filters (1.5 or 2.0 log units) have been used by several researchers (Owsley et al., 2016a; Pondorfer et al., 2020; Sunness et al., 2008; Neely et al., 2017; Owsley and McGwin, 2016; Owsley et al., 2016b; Crosson et al., 2019). Regardless of the method employed, decreasing light levels are related to a decrease in VA (Rabin, 1994; Lin, Ng and Nguyen, 2015; Johnson and Casson, 1995).

2.5 Visual Acuity and Age

Ageing can be divided into primary ageing and secondary ageing. The anatomical and physiological changes associated with the ageing process without the presence of disease is called primary ageing (Holloszy, 2000). Secondary ageing is caused by treatable diseases, social problems, psychological difficulties and economic stress (Holloszy, 2000). The primary objective of this study is to establish the effect of normal (primary) ageing on VA and CSF. Many studies have investigated the prevalence of age-related eye diseases and associated visual impairment, but visual performance in healthy elderly is much less investigated. In clinical practice it is of importance to separate the effect of normal ageing from the effect of disease on visual performance. In routine clinical practice, VA is often used to determine visual performance of the patients. Therefore, knowledge about the effect of normal ageing is essential.

2.5.1 Photopic Visual Acuity and Age

VA measurements are mainly performed at high contrast under photopic circumstances. Normal ageing also affects photopic VA (Martínez-Roda et al., 2016; Frisén and Frisén, 1981; Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Radner and Benesch, 2019; Elliott, Yang and Whitaker, 1995). Haegerstrom-Portnoy et al. (1999) found that high contrast VA under photopic conditions decreased slightly with age (Haegerstrom-Portnoy, Schneck and Brabyn, 1999). However, they found that variability in VA measurements increased with age. The study enrolled 900 participants between the ages of 55 to 102 years. This finding is in agreement with a broad range of other visual function measurements in ageing. Haegerstrom-Portnoy

et al. (1999) measured VA with the Bailey-Lovie high contrast chart using testing a testing distance of 10 ft (3.05 m). Ocular, or systemic conditions that could affect visual performance, were not an exclusion criterion. All participants wore their habitual correction. The results were also analysed by combining them with results from other studies. The results of the different studies combined together (34,713 participants), are in agreement till the age of 70 years. Most studies found good high contrast VA until the age of 70, at which point VA starts to decrease more rapidly. The Bailey-Lovie test chart was also used in a prospective study to establish age-related changes in VA (Martínez-Roda et al., 2016). In this study 198 participants in four different age groups (31-40, 41-50, 51-60 and 61-70) were recruited. A full eye examination was conducted and participants with ocular conditions and lens opacities other than nuclear sclerotic changes were excluded from the analysis. The performance of the remaining 102 participants showed stable VA thresholds till the age of 50, thereafter VA decreased, which was more pronounced in the last decade. In another study, the effect of ageing on monocular VA was established in 100 participants with a newly developed test chart at 4m (Frisén and Frisén, 1981). In this study an eye examination was carried out to exclude participants with ocular disorders. However, lens opacities can affect VA and these were not graded. Alternatively, visibility of the papillomacular bundle of the retinal nerve fibre layer with red-free ophthalmoscopy was used as an inclusion criterion. The participants were provided with best correction and had the opportunity to continue viewing the chart without a time limit. The chart illuminance was 400 cd/m^2 and the test letter luminance was 25 cd/m^2. The researchers found an improvement in VA thresholds till the age of 25 and a gradual decrease thereafter. In some studies, data were collated from previous research projects, sometimes completed with additional participants. In one such study, 42 participants were added to the data of three previous studies, resulting in 223 participants in the age range of 18 to 80 years (Elliott, Yang and Whitaker, 1995). Mean VA thresholds showed an improvement between the age ranges of 18-24 and 25-29 years and gradually decreased afterwards. In a subsequent study with data collated from previous studies, a significant decrease of VA was found from middle age (Sjöstrand et al., 2011). The effect of healthy ageing on photopic VA was analysed by combining the data of Elliott et al. (Elliott, Yang and Whitaker, 1995), Frisén & Frisén (Frisén and Frisén, 1981), a population sample of Gothenburg, Sweden (70-82 years) and a population from Oulu, Finland (82 or 88 years). In the Oulu study, VA was measured with the E-chart (180-200 cd/m^2) at a test distance of 6 m and in the Gothenburg study with the Monoyer-Gräntström letter chart (500 cd/m^2) at a test distance of 5 m. The different

tests and methods used can affect the results. Most of the participants had thresholds better than 6/6. To detect early deterioration in VA, test charts need more acuity levels beyond 6/6. In a recent study by Radner and Benesch (2019), age-related changes with the ETDRS 2000 charts was established (Radner and Benesch, 2019). A thorough eye examination was conducted on 200 participants, including history taking, refraction to evaluate the best possible prescription for testing distance, slit lamp examination, Goldman tonometry, funduscopy and Humphrey 30.2 SITA fast visual field examination. The ETDRS 2000 charts 1 and 2 were mounted in a standardized illumination (160 cd/m^2) cabinet to establish VA at a testing distance of 4 m. The best-corrected logMAR VA was evaluated after attempting to read single letters of the row where participants stated that they could not read letters. The mean VA thresholds per age range of 5 years were stable till the age of 55-59 and decreased after this break-point. Up until the age of 64, all VA thresholds were better than 0.0 logMAR (smaller than 1 minutes of arc).
In summary, previous studies found a decline in photopic VA beyond ~60 years of age. The different test charts designs, test illuminance, number of different examiners, tests included in eye examination, inclusion and exclusion criteria, best correction or habitual glasses and definition of a normal healthy observer must be taken into consideration. Therefore, it is difficult to compare the results of the different studies performed.

2.5.2 Mesopic Visual Acuity and Age

In many western countries, the retirement age is increasing, for example the retirement age in the UK is placed now at 67, which was previously 60 for women and 65 for men (Keeble-Ramsay, 2018). Furthermore, lower fertility rates and an increase in life expectancy are contributing to an expanding older working population (Keeble-Ramsay, 2018).
It is well established that older individuals need more light to carry out visual tasks that younger people can carry out comfortably at lower light levels (Hammond et al., 2019). This is especially important in visually demanding occupational settings, like lorry drivers or pilots, where minimum levels of VA are required. Although visual complaints in mesopic conditions are common, VA is not routinely measured in mesopic light levels. Only a few studies have investigated the effects of normal healthy ageing on VA in mesopic conditions. Photopic (90 cd/m^2) and mesopic (1 cd/m^2) VA were measured with the Bailey-Lovie chart placed at a distance of 4m in a study to investigate the relationship between macular thickness and photopic and

mesopic VA in healthy participants (Puell, Pérez-Carrasco and Palomo Alvarez, 2019). Participants were divided into two groups; 38 healthy young (mean age 22.3 ± 2.5) and 39 healthy older (mean age 62.1 ± 3.6) participants. Participants with abnormal findings during ophthalmological examination, systemic diseases and cataract gradings higher than 2 on the LOCS III classification system were excluded. Photopic and mesopic VA thresholds were significantly better in healthy young individuals in comparison to healthy older individuals. The difference was more pronounced in mesopic light conditions. The results of the macular layer (inner and outer retinal layer) thickness measured using OCT revealed a relationship between greater macular thickness and worse mesopic VA in healthy individuals.

The studies reported in this chapter describe numerous tests available for the measurement of VA, a majority of which lack standardized protocols for use in clinical practice, particularly for measurements under mesopic conditions. Previous research has established that photopic VA slightly decreases with age (Haegerstrom-Portnoy et al., 2000), and the difference between photopic and mesopic VA is more pronounced in elder individuals (Puell, Pérez-Carrasco and Palomo Alvarez, 2019).

3. Contrast Sensitivity

3.1 Introduction to Contrast Sensitivity

In addition to VA, contrast sensitivity (CS) also yields useful information on the kind of spatial vision one can achieve. CS refers to the ability to distinguish between fine increments of light versus dark and is obtained by measuring the smallest amount of contrast needed to detect a target. CS is defined as the reciprocal of the contrast threshold and can be measured in spatial and temporal CS. Figure 3.1 illustrates the sinusoidal grating spatial CSF and shows from left to right increasing spatial frequencies and from top to bottom increasing contrast. The inverted U region over which the stripes are visible demonstrates our window of visibility. Temporal CS can be determined by measuring sensitivity to contrast as a function of time. With temporal CS testing a sinusoidally stimuli varying over time is presented. The depth of modulation and presentation rate are determined for the visibility of the temporal modulated stimuli. In this study we will concentrate on the spatial CSF.

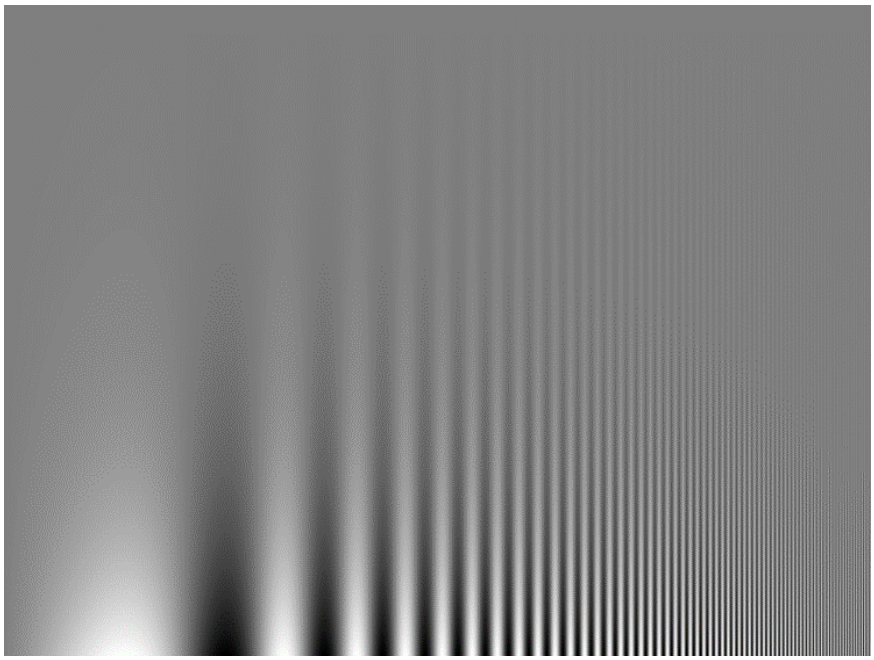


Figure 3.1 Demonstration of the contrast sensitivity function. Contrast increases from top to bottom and spatial frequency increases from left to right. Developed by Campbell and Robson (Campbell and Robson, 1968).

CS is of importance in everyday life as objects and their backgrounds tend to be of varying contrasts. Therefore, CS provides a better prediction of seeing real objects than VA (Owsley and Sloane, 1987; Jindra and Zemon, 1989). VA measurements in clinical practice use high contrast and therefore do not characterize the whole spatial cycle. Many patients have good VA but may be visually impaired in real-life situations. CSF improves by increasing the retinal illuminance. This effect is more pronounced in the mesopic range than the photopic range. Retinal illuminance in larger pupils is greater than for eyes with a small pupil. However, not all the light enters the eye through the pupil's centre (Stiles and Crawford, 1933). Light entering the peripheral part of the pupil is not as bright as that passing through the centre. This phenomenon, called Stiles-Crawford effect decreases the retinal illuminance for light entering the cones transversely. The large pupil size in low light levels also contributes to an increase in higher-order aberrations. Point spread function is the intensity with which an optical system focuses an image from a point source on the retina. The larger the pupil, the greater the increase in the blurring of the point source. However, under mesopic conditions the neural CS is decreased and therefore the effect of higher-order aberrations is limited (Dalimier, Dainty and Barbur, 2008). In photopic conditions, no large aberrations are expected if the pupil size is small. Light scatter also has an effect on retinal illuminance and CS. Retinal illuminance increases with light scatter, however CS decreases. The contrast and thus the visibility of the target is reduced by the veil of luminance formed by scattered light. Many studies have found an increase in light scatter with age (Harrison et al., 1993; Puell et al., 2004a). This progression is more pronounced from the age of 45 (Hennelly et al., 1998). Retinal sensitivity increases with increasing luminance (Barbur and Stockman, 2010); however, the addition of light from light scatter is not advantageous for contrast. Lens opacities (cataract) are an important causative factor for light scatter. More advanced cataracts will result in increased light scatter. The classification of cataracts is significantly related to light scatter values (Siik et al., 1999).

Furthermore, the best optical correction for the test distance must be provided. Optical blur can affect CS significantly, and if participants wear their habitual correction, it is not guaranteed that this is also their best optical correction. Both VA and CSF are affected by optical defocus (Rabin, 1994), but the effect is more pronounced in CSF (Woods, Strang and Atchison, 2000). The decrease in CSF as a result of optical defocus can mimic the decrease found in ocular disease. In clinical practice, best correction is normally determined at 6 meters, however, the test distance of VA and CSF often differ. Multifocal glasses, often provided to elder

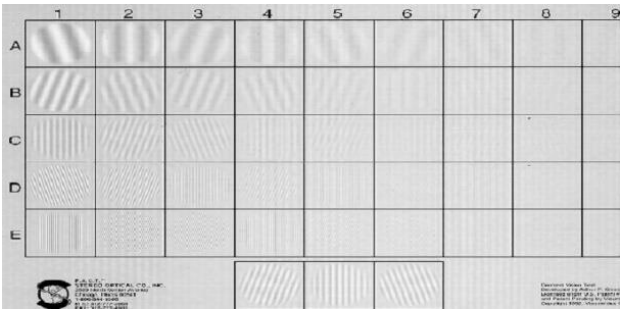
individuals, can also decrease CSF because of distortion or incorrect adjustment of the glasses (Lord, Dayhew and Howland, 2002).
Retinal illuminance is not the only factor accounting for a decline in CS. Previous researchers have suggested that neural retinal and visual pathway changes caused by normal ageing or retinal disease contribute to a reduction in CS (Curcio et al., 1993; Gao and Hollyfield, 1992).

3.2 The measurement of Contrast Sensitivity

CS tests fall into two broad groups depending on whether threshold contrasts are measured using spatially-periodic sinusoidal gratings or single optotypes, resulting in vastly different outcomes. Grating CS charts employ sinusoidal or square-wave gratings that vary in contrast and size, such as the Functional Acuity Contrast Test (FACT; Stereooptical Company, Inc., Chigago, US), CSV-1000 (VectorVision, Houston, Texas, US) and Vistech (Vistech, Dayton, Ohio, US). The thresholds are measured as a function of spatial frequency and represent the smallest grating contrast needed to detect anything different to a uniform field. Full measurements of CS with sinusoidal gratings as a function of spatial frequency and visual field size yield a great deal of useful information, but take a long time to carry out, and the results depend on the mode of stimulus presentation (e.g., briefly presented or drifting gratings) and the participant's threshold criterion (e.g., just noticeable bright or dark bars, motion direction, local flicker or just anything different to a uniform field) (Kelly, 1977; Rijsdijk, Kroon and van der Wildt, 1980). These disadvantages, particularly the long testing times, make full CS tests unattractive for use in the clinic. Letter contrast sensitivity, also named FCS, is measured by correct naming of letters or gap location in Landolt rings of varying contrast, such as the Pelli-Robson test (Pelli, Robson and Wilkins, 1988). The fixed optotypes in these tests are normally three times greater than the VA threshold. These tests are quicker to carry out and often easier to understand for patients if letters and Landolt C rings are more familiar for them. Letter contrast sensitivity is less sensitive to spatial aliasing and spurious resolution than grating contrast sensitivity (Wang, Bradley and Thibos, 1997; Herse and Bedell, 1989). In addition, letter contrast sensitivity can be used to separate the effects of negative and positive contrast which are confounded in grating stimuli.

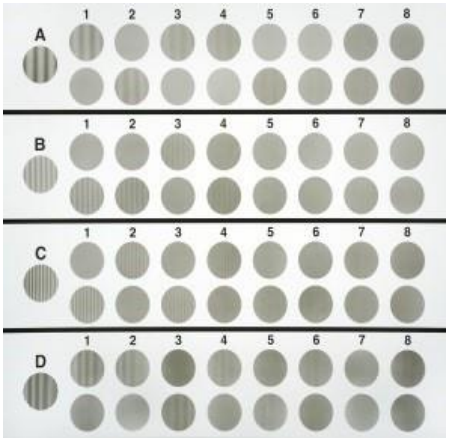
3.3 Photopic Contrast Sensitivity

Despite not being a routine examination in clinical practice, several tests are available to measure photopic CS. For example the FACT test which consists of 5 different sinusoidal grating frequencies and 9 levels of contrast. The patient reports the last grating seen for each row allowing determination of the CSF. The Bailey-Lovie chart is available in both high- and low contrast and the same number of letters and constant spacing is used for each row (Bailey and Lovie, 1976). With the Bailey-Lovie chart sensitivity along the high frequency limb of the CSF is determined and measured in log of minimum angle of resolution (logMAR). The Regan contrast letter charts provides information about sensitivity in the same way as the Bailey-Lovie chart (Regan, 1988; Regan and Neima, 1983). Both tests measure acuity thresholds for different contrast levels. However, the Bailey-Lovie chart is available in two contrast levels (100% and 18%) and the Regan chart in five contrast levels (96%, 50%, 25%, 11% and 4%). A widely used CS test is the CSV-1000E which provides four rows of sine wave gratings. These gratings test the spatial frequencies of 3, 7, 12 and 18 cycles/degree. This test is useful in evaluation of eye disease and is easy to perform. Different variants of the CSV-1000E are available; the CSV-1000RS for screening refractive surgery patients, CSV-1000S for cataract screening, CSV-1000CVA to measure both CS and low contrast acuity, CSV-1000 LAN C with Landolt C format and the CSV 1000 1,5 CPD which is designed for food and drug clinical trials. A more popular and frequently used test in research is the Pelli-Robson CS sensitivity chart (Clement Clarke, Inc., London, United Kingdom) (Pelli, Robson and Wilkins, 1988). Each row consists of 6 letters divided into two triplets. All the letters have the same size, and contrast reduces with each triplet, 16 in total. The CS is determined by the faintest triplet out of which at least two letters are correctly identified. The MARS (Mars Perceptrix a Corporation, Chappaqua, US) contrast test has a similar design to the Pelli-Robson chart (Dougherty, Flom and Bullimore, 2005). However, there are some differences between both tests. The MARS chart is printed on plastic and performed at 0.5m, in contrast with the Pelli-Robson chart printed on cardboard and carried out at 1m. With the Pelli-Robson test, the contrast decreases per triplet from 100% to 0.56%. The MARS chart consists of eight rows with six letters, and contrast decreases with each letter by a factor of 0.04 log units (contrast varies from 91% to 1.2%). Figure 3.2 (A-D) shows some different available CS tests.



(A)

(B)



(C)

(D)

Figure 3.2 (A-D) The Functional Acuity Contrast Test (FACT CS Test) (image courtesy of Stereo Optical) (A), MARS test (image courtesy of Precision Vision) (B), CSV-1000E contrast test (image courtesy of VectorVision) (C), Pelli-Robson chart (image courtesy of Precision Vision) (D).

3.4 Mesopic Contrast Sensitivity

In clinical settings mesopic CS measurements are rarely measured. As with the effect of mesopic luminance levels on VA, FCS also decreases at lower luminance levels (Rabin, 1994). In Rabin's study the effect of luminance on monocular VA and small letter contrast was investigated (Rabin, 1994). Both VA and CS were measured with a computer-generated letter chart displayed on a monitor. These charts were based on the Bailey-Lovie VA and Pelli-Robson CS charts. VA was measured with 93% contrast letters which became progressively smaller in 0.1 log unit steps. CS performance was established with a letter chart using a constant letter size (6/7.5) but with a decrease in contrast of 0.1 log unit for each line (from 93% to 5% contrast). Decreasing the luminance level from 116 cd/m^2 (photopic) to

0.23 cd/m^2 (mesopic) by neutral density filters resulted in a three times reduction of VA, and 17 times reduction of CS. In another study, the results of monocular mesopic CS measured with the Mesotest (Oculus, Germany) were compared with the photopic CS results with the MARS charts and the Freiburg Acuity and Contrast Test (Hertenstein et al., 2016).The mesopic luminance level with the Mesotest is 0.032 cd/m^2 and the central stimuli consist of a Landolt C with an equivalent VA of 0.1 in decimals. Better photopic CS thresholds were found compared with mesopic CS, in all groups; healthy participants, glaucoma patients and cataract patients. Another interesting finding from this study; good mesopic CS predicted good performance with photopic CS, although good photopic CS is not always associated with good mesopic CS (Hertenstein et al., 2016). However, the photopic and mesopic CS were established with different tests and therefore less comparable. In some studies, photopic and mesopic CS were measured with the same test (Puell et al., 2004b; Haughom and Strand, 2013). For example, Puell et al. (2004) measured binocular CS with the Pelli-Robson chart in photopic (85 cd/m^2) and mesopic conditions (0.15 cd/m^2). In each decade, thresholds in the photopic condition were significantly better in comparison with mesopic conditions. These binocular results can explain patients' complaints in low illuminance levels. However, in the screening of early ocular disease, monocular results are of more interest. Haughom and Strand (2013) measured CS at five frequencies in 197 young (age range 17-54) individuals with the Optec 6500/FACT (Stereo Optical Co., Inc., Chicago, IL, USA) in both photopic (85 cd/m^2) and mesopic (3 cd/m^2) conditions (Haughom and Strand, 2013). The performance in photopic conditions was significantly better compared with the mesopic results. These results confirmed the need for separate photopic and mesopic CS reference values.
Mesopic CS is also of benefit in visually demanding occupational environments when normal limits of spatial vision in low illuminance levels are required. In addition, measurements in mesopic conditions seem to be more sensitive at differentiating between candidates, for medical selection purposes, for example in military (Koefoed et al., 2015).

3.5 Contrast Sensitivity and Age

Previous studies have found good correlation between CS and the level of comfort and visual performance one can achieve in routine daily tasks (Wai et al., 2021; Freeman et al., 2006; Owsley and McGwin, 2010; Brown, 1981; West et al., 2002). CS is more sensitive to changes in retinal image quality caused by the optics of the

eye, when compared to VA. However, a decrease in both VA and CS can also be attributed to neural changes with increasing age caused by loss of photoreceptors and reduction in cone sensitivities (Werner and Steele, 1988), reduced photon absorption efficiency in cones (Silvestre, Arleo and Allard, 2019), and/or neural changes in the retina caused by normal ageing and/or disease (Wai et al., 2021; Maynard, Zele and Feigl, 2016; Müller et al., 2019; Bittner and Ferraz, 2020; Midena et al., 1997; Roh et al., 2018; Gillespie-Gallery et al., 2013; Pondorfer et al., 2020; Feigl et al., 2011; Kleiner et al., 1988). Normal age-related limits are of importance to separate the effect of normal ageing from disease.

3.5.1 Photopic Contrast Sensitivity and Age

Many studies have shown that CS measurement is a more comprehensive method to obtain visual performance information than VA (Elliott, 1987; Puell et al., 2004b; Ross, Clarke and Bron, 1985; Sloane, Owsley and Alvarez, 1988). Therefore, knowledge about the effect of age on CS is of importance, in particular in an ageing population with increasing retirement age. The Pelli-Robson chart was used in a study to establish normal age-related values of CS in both photopic and mesopic conditions (Puell et al., 2004b). In this study, 292 participants divided into six age groups were assessed by an ophthalmological exam, but the inclusion criteria were not described. The photopic measurements were taken binocularly at an illuminance level of 85 cd/m^2. Mean CS thresholds were stable till the age of 60 and gradually decreased after that. These results are in agreement with the findings of another study with the Pelli-Robson chart (Mäntyjärvi and Laitinen, 2001). In this study, with 87 participants, binocular and monocular CS thresholds in photopic conditions (85 cd/m^2) were measured (Mäntyjärvi and Laitinen, 2001). Participants were divided in 7 age groups, and each group consisted of ~ 12 participants. Monocular thresholds were lower in comparison with binocular thresholds, although the decrease after the age of 60 was similar for monocular and binocular thresholds. In contrast, with the same Pelli-Robson chart a decrease after the age of 50 was found in another study (Elliott and Whitaker, 1992). This could be a result of different inclusion and exclusion criteria. In Elliott and Whitaker's study (1992), the decline in CS was also found with the Vistech CS system and the Cambridge low contrast gratings test (Elliott and Whitaker, 1992). The decline of CS with age is more pronounced at higher spatial frequencies (Sia et al., 2013; Ross, Clarke and Bron, 1985). However, statistically significant differences at all spatial frequencies were found with the CSV-1000 contrast test (VectorVision, Greenville, Ohio, US) between subsequent five

years age range groups from the age of 45 years in an Australian male population (Sia et al., 2013). In studies by Derefeldt et al. (1979) and Ross et al. (1985), participants were divided into three (6-10, 20-40 and 60-70 years) and two age groups (20-30 and 50-87 years), respectively. There was no statistical difference between the young and middle-aged groups in FCS thresholds. However, the measured differences were statistically significant for the middle and high frequencies when comparing the younger and the oldest age groups (Derefeldt, Lennerstrand and Lundh, 1979; Ross, Clarke and Bron, 1985). This agrees with another study where no significant differences were found in a sample of 90 middle-aged participants (Harrison et al., 1993). However, the evaluation of just a few groups did not provide normal values for each age. The CSV-1000E contrast test (VectorVision, Greenville, Ohio, US) was also used in a study to establish photopic FCS at frequencies 3, 6, 12 and 18 cycles per degree (CPD) in 102 participants with an age range of 31-70 years (Martínez-Roda et al., 2016). In this study, CS remained stable until 50 and decreased significantly thereafter at higher spatial frequencies.

Most reports indicate a decrease of CS with age, however, the results of different studies are somewhat inconsistent (Derefeldt, Lennerstrand and Lundh, 1979; Gillespie-Gallery et al., 2013; Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Harrison et al., 1993; Puell et al., 2004b). The differences could be due to the age range of the participants. Photopic CS declined from the age of 60, and some studies only included participants till middle age (Harrison et al., 1993), or a small number of elderly participants were participating.

3.5.2 Mesopic Contrast Sensitivity and Age

With age, the decline in CS is more pronounced in mesopic conditions (Sloane, Owsley and Alvarez, 1988; Puell et al., 2004b). Puell et al. (2004) showed that mesopic CS declines from the age of 50, one decade earlier in comparison with photopic CS (Puell et al., 2004b). This could be induced by the reduction of rods at the parafovea with age (Curcio et al., 1993; Gao and Hollyfield, 1992). In this study, CS was measured using the Pelli-Robson chart binocularly in photopic (85 cd/m^2) and mesopic conditions (0.1 to 0.2 cd/m^2). All six age groups showed significantly better CS thresholds in photopic conditions compared with mesopic conditions. In a more recent study, binocular photopic and mesopic CS were measured with the Pelli-Robson chart (Maynard, Zele and Feigl, 2016). The age of the 73 healthy participants ranged from 19-85 years. The results were consistent with the previous

findings of Puell et al. (2004), a significant decline with age in both photopic and mesopic conditions. In the comparison between young individuals (mean age 24) with older (mean age 73), significantly better monocular CS results were obtained in the younger individuals (Sloane, Owsley and Alvarez, 1988). These results showed the difference between young and old participants, but not the continuous effect of ageing on CS from young to old. Gillespie-Gallery et al. (2013) measured foveal and parafoveal contrast thresholds at different illuminance levels (34, 7.6, 3.2, 1.2 and 0.12 cd/m$^{2)}$ (Gillespie-Gallery et al., 2013). A decline in CS was found with age and decreasing illuminance levels, and the age-related decrease was markedly more in the parafoveal region.

Under mesopic conditions, the decline in mesopic CS started at an earlier age (Puell et al., 2004b; Maynard, Zele and Feigl, 2016; Mäntyjärvi and Laitinen, 2001) as a result of pupil miosis, increased light scatter and absorption of light by the lens and some retinal and neural changes (Curcio et al., 1993; Elliott, 1987; Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Elliott, Whitaker and MacVeigh, 1990). The age-related decline in rod photoreceptor density is well documented (Curcio et al. 1993), and post-receptoral changes, such as loss of ganglion cells and damage to their retinal axons contribute to the worsening of spatial vision in normal ageing (Calkins, 2013).

3.6 Summary of key findings from the literature review

Chapters 2 and 3 provide an overview of measurements and the effect of ageing on VA and CS, respectively. Previous studies concluded an age-related decrease in VA and CS thresholds. The difference between photopic and mesopic CS thresholds is more pronounced in elder individuals**.** However, different protocols are used for the inclusion of participants. The eye examinations ranged from limited to more extensive, and different inclusion and exclusion criteria were used. Furthermore, in some studies the participants wear their habitual corrections, which does not always produce BCVA. Most studies investigated the differences in VA and CS between age groups and did not establish age-related lower and upper limits. The use of different tests for VA and CS and photopic and mesopic conditions make the results less comparable. In addition, the normal age-related VA and CS thresholds were often established per decade and not for each age separately. Most studies established only normal monocular or binocular VA and CS values. However, normal age-related limits are of interest, in both monocular and binocular viewing. The monocular results are particularly of interest in the early detection of ocular

disease, and the binocular results in occupational settings and to estimate visual performance in different light conditions. VA and FCS are usually measured with negative contrast optotypes in clinical practice. Although, positive contrast optotypes may be more sensitive in the early detection of ocular disease in comparison with negative contrast.

The current study will obtain boundaries for healthy aging of spatial vision under both photopic and mesopic lighting for the 16 different stimulus conditions. Equations will be produced that describe normal aging limits and full measures of variability in spatial vision using monocular and binocular thresholds measured with negative and positive contrast. This study will establish the expected age limits of spatial vision for monocular and binocular viewing under photopic and high mesopic lighting with both positive and negative optotypes. To the best of our knowledge this is the first study using a single test, which can be implemented immediately either in the clinic or in an occupational setting.

4. Materials and Methods

This chapter describes the recruitment process, the full eye examination, the procedures used to investigate photopic and mesopic VA and FCS, the criteria selected to screen for normal healthy participants and the combination of statistical methods employed in the analysis of the results.

4.1 Participant recruitment

A total of 382 participants, age range 10 to 90 years, were recruited at three different sites in the Netherlands: (1) private eye clinic, Damme Optometrie in Kesteren, (2) the University Eye clinic at the University of Applied Sciences, Utrecht, and (3) employees at the City Hall of Alphen aan den Rijn. The inclusion of a primary care setting, educational institution and workplace environment was a conscious choice to maximize random sampling in diverse populations. Table 4.1 shows the total number of participants recruited per decade, including the mean age and standard deviation. The participants were invited to take part by the researcher or one of his colleagues.

The study was approved by the Research and Ethics Committee at City, University of London, and the Medical Ethics Committee at the University Medical Centre, Utrecht, Netherlands. The research followed the tenets of the declaration of Helsinki. All participants were given an information sheet at least a few days prior to their appointment so that they had enough time to consider participation. For each testing site, three different information sheets were available, one for each age group: 10-11 years, 12-15 years, and 16-90 years (Appendix B, D, F, H, J, L and N). The different information sheets for specific age groups are based on Dutch ethical regulations (CCMO, 2021). Prior to participating in the study, participants had the opportunity to ask questions to the investigator and/or an independent person as per research and ethical guidelines in the Netherlands. The independent person was an optometrist and low vision specialist at a rehabilitation centre for the visually impaired and was experienced in CS measurements and eye examinations. All participants provided written consent (Appendix C, E, G, I, K, M and O). In cases where participants were younger than 16 years old, the consent form was signed by the participant's parents/legal guardians (10-11 years) or by the participant (child) and their parents/legal guardians (12-15 years). In the case of minors, especially if

the participant was under the age of 15 years, the parent/guardian was encouraged to be present during the examination. The presence of the parent/guardian was to elicit an accurate history and symptoms as well as for safeguarding the child.

	Number of participants (n)	Mean age (M ± SD)
Total	382	46.68 ± 19.85
Decade 1 (10-19 years)	49	14.37 ± 2.97
Decade 2 (20-29 years)	49	25.25 ± 2.89
Decade 3 (30-39 years)	39	34.43 ± 2.57
Decade 4 (40-49 years)	55	44.81 ± 2.80
Decade 5 (50-59 years)	73	54.60 ± 2.65
Decade 6 (60-69 years)	69	64.60 ± 2.65
Decade 7 (70-79 years)	39	73.52 ± 3.00
Decade 8 (80-89 years)	9	82.93 ± 2.20

Table 4.1 Total number of recruited participants, including numbers per decade, mean age (M) and standard deviation (SD).

4.2 Estimation of sample size

Prior to deciding on the sample size for the current study a relevant review of the literature was carried out in order to determine what was an appropriate sample size. The effectiveness of sample size calculations for clinical research studies depends largely on the validity of preliminary results and the assumptions involved. Estimates of appropriate sample size vary greatly even when similar research studies are involved. Calculations are often based on binomial distributions with a fixed probability of success per sample, even when considerable variability is expected within each population. When the analysis of the expected results relies on non-parametric tests, the choice of sample size becomes even more variable. For example, when blood tests are involved, a sample of ~ 120 is often employed (Burtis and Bruns, 2007). However, not all statisticians agree and argue in favour of either larger or smaller sample sizes. Different sample sizes have often been used when determining normal limits for diagnostic instruments involved in vision care (Leslie and Greenberg, 1991; Lott et al., 1992; Wellek et al., 2014) depending on the assumed within and inter-subject variabilities and the comparisons with previous studies. For example, the range of sample sizes in studies establishing normal limits for OCT (Optical Coherence Tomography), HVFA (Humphrey Visual Field Analyser) and CAD (Colour Assessment and Diagnosis test) varies between 53 to 399 participants (Bengtsson and Heijl, 1999; Bengtsson and Heijl, 2003; Chaglasian et

al., 2018). Heijl, who has investigated the normal limits of HVFA tests on numerous occasions, recommends a sample size of a couple of hundred participants covering all ages (A. Heijl, Personal Communication, September 4, 2018). This is in agreement with the findings of a previous study to establish the number of participants required for establishing a normative database in VF (Visual Field) (Phu et al., 2018).

Following a review of the literature and examination of previous studies on the effects of ageing carried out at City University (Barbur and Konstantakopoulou, 2012; Gillespie-Gallery et al., 2013) the decision was taken to aim for at least 380 participants to ensure that following screening, the remaining sample size would be sufficient to represent adequately the average performance within each decade. The aim was to recruit ~ 50 participants for the first six decades and ~ 40 participants for the last two decades. However, for the last decade, this number of participants turned out to be too optimistic due to very few individuals in this age range being classed as normal. Participants with ocular conditions, such as age-related macular degeneration (AMD) and glaucoma and systemic conditions which are expected to affect spatial vision such as diabetes were not included in the final sample to be used in the analysis of normal limits of spatial vision. These groups of participants were not excluded from the study, but their results were analysed separately and then compared with the age-related normal limits.

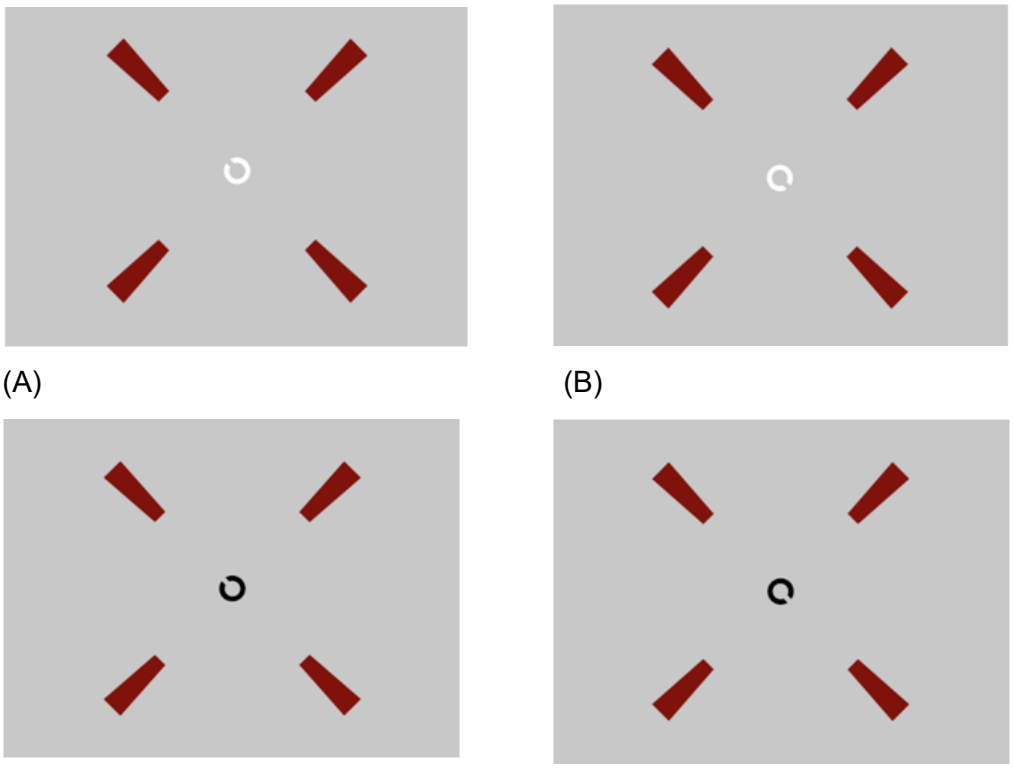
4.3 Acuity *Plus* test

High contrast VA and FCS with optotypes of both positive and negative contrast were measured in each participant using the Acuity-*Plus* test (City Occupational Ltd., London, United Kingdom). This test of spatial vision is one of a series of Advanced Vision and Optometric Tests (AVOT) developed at City, University of London for use in occupational health and in the clinic (Chisholm et al., 2003). The test was initially designed to assess the effects of corneal refractive surgery on visual performance under photopic and mesopic lighting (Chisholm et al., 2003) and has more recently undergone improvements in stimulus parameters and methodology. Each standard protocol measures four parameters of interest which provide useful information on the participants' spatial vision. The Acuity-*Plus* test employs a stable, high resolution, 10-bit dynamic range visual display (NEC Spectraview 2690WU, NEC, Tokyo, Japan), which the participant views from a distance of 3m. The display is fitted with a hood to minimise ambient lighting, and initial adjustments are carried out by the manufacturer to minimise the black light

level and to achieve a maximum luminance of ~ 146 cd/m^2 in native colour mode. The display was turned on 20 minutes before tests were carried out to make sure the luminance was stable. The manual of the LCD display advises 20 minutes warm up time to allow maximum performance. Furthermore, the stimulus display was checked for luminance calibration periodically and recalibration of each primary colour was performed when required. A high-performance laptop drove the display via a VESA DisplayPort interface which supports 10-bit output graphics as needed to match the dynamic range of the visual display. All participants performed the Acuity-*Plus* test with full updated correction for the testing distance of 3m, which was provided in a trial frame, to ensure that testing conditions for all participants were equivalent with respect to spectacle properties. The room was completely darkened at all three locations and the low mesopic ambient lighting was attributed to the light produced by the operator's monitor and the stimulus background field on the visual display. This ensured that the ambient lighting remained very similar across the three testing sites.

The VA and FCS thresholds were measured using a four-alternative, spatially-aided, forced-choice procedure based on four, randomly interleaved, two-up/one-down, staircases with variable step sizes. Using this approach, the chance probability of a correct response is 1/16 and the measured threshold represents the signal strength needed to produce 71% correct response. The interleaved measurements of four variables in the same test minimizes the effects of other factors such as fatigue and pupil size changes. The stimulus consisted of a Landolt C optotype with the gap positioned randomly in one of the four quadrants and each test measured four parameters, i.e., VA and FCS with both positive and negative contrast. Figure 4.1 (A-D) shows screenshots of Landolt ring stimuli of both positive and negative contrast polarity and varying gap orientations. The choice of optotype and optimum size have evolved over several years. Landolt rings with an outer diameter of functionally important are frequently employed in such tests, largely because a gap size of 3 min arc is considered functionally important in almost every occupation and at the same time is large enough to ensure that the majority of individuals can carry out the task, even when the retinal image quality is affected by small residual refractive errors, large higher order aberrations and scattered light. A Landolt C optotype has additional advantages in that a four-alternative, forced response procedure can be implemented in a two-down, one-up staircase (Levitt, 1971), with variable step sizes which results in low chance probability (i.e., 1/16) and the thresholds measured correspond to 71% probability of a correct response. This test procedure is statistically efficient and its implementation on calibrated visual displays

which allow for the use of both luminance increments and decrements make this measurement of functional FCS appropriate for use in both occupations as well as in the clinic (Chisholm et al., 2003; Gillespie-Gallery et al., 2013).



(A) (B)

(C) (D)

Figure 4.1 (A-D) Screenshots of possible Landolt C test stimuli in positive (A+B) and negative (C+D) contrast.

In all measurements, the participant had to detect and 'register' the location of the gap in the Landolt C optotype. A short beep at the end of each stimulus presentation prompted the participant to press one of the four raised buttons on the numeric keypad (figure 4.2 A) to report the perceived location of the gap. When unsure about the gap's location, the participant's instruction was to guess the most likely location without hesitation. Between presentations of the stimulus, a fixation cross was displayed so that the participant maintained central fixation. Both photopic and mesopic spatial vision was assessed using the standard mesopic and photopic protocols in the Acuity-*Plus* test. The mesopic protocol was always preceded by ~ 10 minutes of adaptation to the low luminance screen employed in the mesopic condition. For this protocol, the participants wore spectrally calibrated, 'neutral density' sunglasses (Oakley Garage Rock, Oakley Inc., Lake Forest, California, USA). The program employed the known spectral transmittance of the sunglasses to

ensure that when viewed through the glasses, the stimulus display had the correct luminance and chromaticity.

(A) (B)

Figure 4.2 (A-B) Numeric keypad with four bespoke response buttons (A) and the L-1009 luminance meter (B) From https://hofeka.hu/en/lighting-laboratory/.

A 'learning mode' option preceded any measurements of VA or FCS. This brief test required 100% correct responses and ensured that every applicant was familiar with and understood the task. Every participant carried out the initial learning test under binocular viewing conditions. The order of testing (monocular, binocular) was randomised for both photopic and mesopic conditions. Participants were seated in a comfortable chair, short breaks separated successive tests to minimise fatigue and the participants were also encouraged to take additional breaks whenever needed during the session. Figure 4.3 shows how the participant's performance was displayed.

VA was measured in minutes of arc and FCS in percentage. The stimulus was presented for 160ms to avoid letter scanning and hence multiple fixations. Moreover, it has been documented that visual processing of a demanding task can be achieved in less than 150ms (Thorpe, Fize and Marlot, 1996). The stimulus was preceded by a briefly presented fixation target designed to capture the participant's point of regard. The disappearance of the fixation target was followed by the Landolt ring stimulus which was presented to the eye centrally. Although a 160ms stimulus presentation time is normally sufficient to carry out the test with little or no improvement with longer presentation times, it is well known that ocular conditions, such as AMD, can require longer stimulus presentation times (Van der Stigchel et al., 2013). Such patients often require much longer times to achieve best acuity compared to age-matched, healthy individuals (Kono and Yamade, 1996). Longer

presentation times also result in multiple fixations and this can aid the self-selection of the least-affected retinal area that yields the highest sensitivity. The use of briefly presented optotypes in VA and FCS tests to eliminate multiple fixations is more likely to reveal spatially localized damage on the retina and poorer temporal responses that can also be attributed to early stage retinal disease.

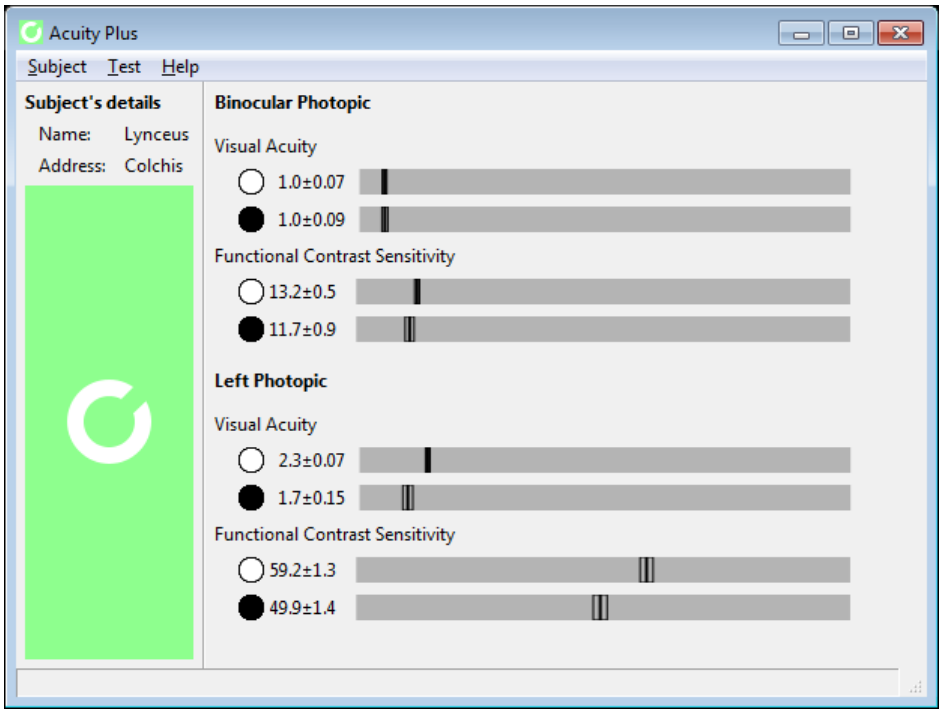


Figure 4.3 Example of presentation of participant's performance From http://www.city-occupational.co.uk/acuity-plus/.

During everyday life and in occupational settings, vision tasks are rarely static, and therefore brief presentation times are also more representative of real-world visual performance (Heinrich et al., 2020). When a short presentation time of 160ms is employed, the majority of normal trichromats achieve a spatial resolution better than one minute of arc (1') acuity, i.e., a Landolt ring size of 5' outer diameter converts to an equivalent Snellen VA of 6/6 and a logMAR VA of 0.0. The conversions from minutes of arc to logMAR are easy to carry out when required. logMAR = $\log_{10}$ (MAR), where MAR is the size of the gap (in minutes of arc) needed at threshold to locate its position. Alternatively, when using the most common Snellen notation, $VA_{Snellen}$ ~ 6/(6*MAR). This means that a Snellen VA of 6/6 corresponds to a MAR of 1'. Doubling this to 2' makes the Snellen acuity 6/12. The data in minutes of arc and percentage were more skewed, in particular in the older age groups. Therefore, the data was transformed in log units to reduce skewness and justify the use of a normal distribution. The VA results in this thesis are presented in logMAR, but also

given in minutes of arc. Many healthcare professionals, in particular in occupational settings, comprehend non logMAR formats more easily (Tsou and Bressler, 2017; Lopes et al., 2011). FCS can be defined in different ways, for example Michelson and Weber contrast. If measurements are made with gratings then the Michelson contrast is preferred, however, when letters or Landolt stimuli are used the Weber contrast is preferred (Pelli and Bex, 2013). The Acuity-*Plus* test defines contrast in percentage utilising the Weber contrast (*Lo*= Luminance optotype, *Lb*= Luminance background):

$$Contrast = \frac{Lo - Lb}{Lb}$$

FCS thresholds were measured in percentage contrast, and transformed to log units for analyses. Throughout the thesis, results are presented in log units. The results in percentage are also given in the interest of the practical application in clinical and occupational settings. The standard photopic protocol measured VA and FCS at the fovea with both positive and negative contrast stimuli for a screen luminance of 32cd/m² and CIE –(x,y) chromaticity coordinates of 0.305, 0.323. The standard mesopic protocol measures the same four parameters using light of the same chromaticity, but with a screen luminance of 2 cd/m². The choice of 2 cd/m^2 for use in the Acuity-*Plus* protocol is representative of typical residential street lighting and other mesopic working environments where adequate spatial vision is required (Wood, 2020; Li et al., 2020). The choice of adapting background luminance was based on typical luminance encountered in mesopic work environments when good spatial vision is still needed in order to carry out visual tasks. Similar light levels are also found in many lit spaces at night and in traffic situations when safety remains an important requirement.

4.3.1 Calibration of the CRT Monitor

The CRT monitor was calibrated at six monthly intervals to ensure correct luminance reproduction for the three primary colours. The automated calibration function of the program Lumcal (City Occupational Ltd., London, UK) was used for luminance calibration. The program contains standard observer CIE values and determined the relationship between the bit values set on the driver card for the red, green, and blue guns and the resulting screen luminance (Wyszecki and Stiles, 2000).
Before calibration, the monitor was ‘warmed up’ for 20 minutes to ensure a steady value of the luminance was reached as per the manufacturer’s guidance. The luminance calibration was used in conjunction with the L-1009 luminance meter

(LMT Lichtmesstechnik, Berlin, Germany)(figure 4.2 B), positioned 1m in front of the monitor and connected to the laptop. Figure 4.4 shows the spectral radiance distribution for the red, green and blue primary colours of the high-performance display employed to carry out the Acuity-*Plus* test. Throughout the study no calibrations issues were identified at any of the testing sites and any deviations, when noted, were within normal limits. The results of one calibration are shown in figure 4.5.

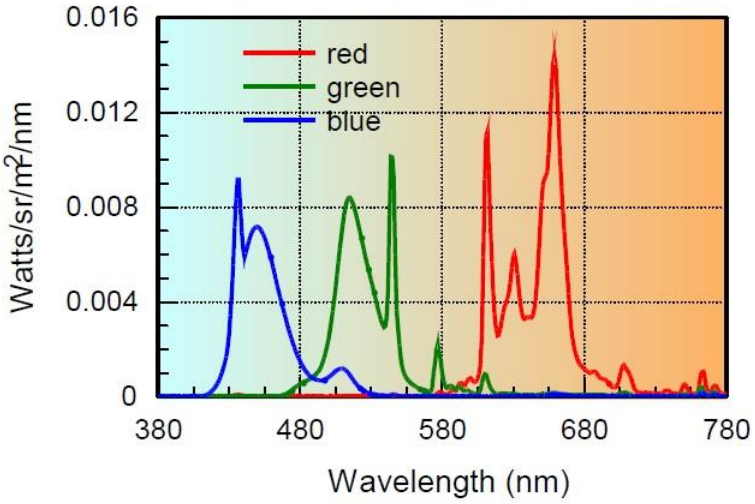


Figure 4.4 Typical spectral radiance distributions for red, green and blue primary colours of the CRT monitor.

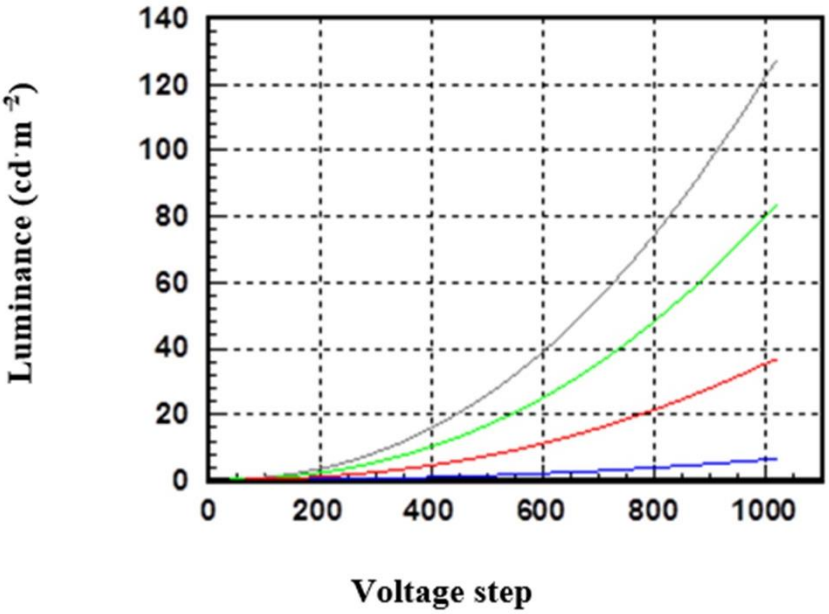


Figure 4.5 Example of one of the calibration results of white, red, green and blue colours.

4.4 Methods

A detailed medical history was taken, all participants or parent/guardian answered questions about their general health, use of medications, ocular health, and general and ocular family history. A full objective and subjective refraction was conducted for a viewing distance of 3m. VA was then measured monocularly and binocularly in logMAR units with the 2000 series revised ETDRS (Early Treatment Diabetic Retinopathy Study) chart 2 (Precision Vision, La Salle, Illinois, USA) using the updated prescription. The original ETDRS illuminator cabinet was used with a background luminance of 160 cd/m^2. The ETDRS chart and illuminator cabinet have become the “gold standard” in VA measurement and are used extensively in research and clinical trials worldwide (Kaiser, 2009). The 3m distance was chosen because the Acuity-*Plus* test was carried out at the same distance. Binocular vision was assessed by the cover/uncover test at distance and near and also with the TNO stereo test (Laméris, Ede, Netherlands). The cover/uncover test is a standard test, carried out in every patient visiting optometric practice and is used to detect eye misalignment. The type of phoria or tropia was detected and the extent measured with a prism bar. The TNO stereo test is an accurate two-dimensional stereo test which is based on random dots and has no monocular cues. It is well established that stereoacuity declines after the age of 50 (Lee and Koo, 2005; Garnham and Sloper, 2006). However, all participants needed to meet the criterion of demonstrating stereoacuity. Participants were tested with the 13th version of the TNO stereo test (van Doorn et al., 2014). Van Doorn et al. (2014) found significantly higher scores with the 13th version of the TNO test compared to the 15th version possibly induced by differences in the printing process and resolution of the pictures (van Doorn et al., 2014). The anterior segment was assessed using a Topcon SL-7F slit lamp (Topcon Medical Japan, Tokyo, Japan) at Damme Optometrie in Kesteren, or a CSO SL9900 5X-D (CSO, Firenze, Italy) slit lamp at the University Eye Clinic (University of Applied Sciences, Utrecht) and the City Hall of Alphen aan den Rijn. The transparency of the lens was noted for each participant and classified according to the Optometric Grading Scales (Pearson, 2003). This scale consists of a set of drawings showing different lens opacities based on the Lens Opacities Classification System III (LOCS III) photographs (Pearson, 2003; Chylack et al., 1993). In this classification system, cataracts are categorized as cortical, nuclear and posterior subcapsular opacifications, and the size or density of the cataracts is indicated using gradings from 1 to 5. The higher the grading, the more severe the stage of the cataracts. When classification tables are based on subjective methods of

assessment, the outcome can be compromised by inter-examiner variability. In order to minimise these effects, all ophthalmic/clinical assessments were performed by the same examiner for all testing sites. The transparency of the cornea was also assessed and participants with corneal oedema, staining, infiltrates as well as participants with corneal degenerations and dystrophies were excluded from the normal participant group. The fundus was assessed by undilated indirect ophthalmoscopy at all locations and photographed with a Topcon TRC-NW65 (Topcon Medical Japan, Tokyo, Japan) non-mydriatic digital retinal camera at Damme Optometrie, Kesteren, or a Canon CX-1 (Canon Singapore Pte. Ltd.) non-mydriatic digital retinal camera at the University Eye Clinic (University of Applied Sciences, Utrecht). At City Hall of Alphen aan den Rijn fundus examination was limited to undilated, indirect ophthalmoscopy due to the unavailability of a fundus camera. All participants had their VA and FCS assessed using the Acuity-*Plus* test which is described in detail in the previous section (see section 4.3). All the clinical tests were carried out once in each participant and took a maximum of one hour to complete.

4.5 Selection of participants for inclusion in the study

The principal aim of this study was to establish mean values and upper normal limits of spatial vision in normal, healthy participants as a function of age. In order to achieve this aim, a number of filters were employed to ensure that the participants included in the study had ‘normal visual performance’ for the corresponding age. Each of the included ‘clinically normal’ participants, fulfilled the following requirements:

1. Absence of medical history of eye or systemic conditions known to affect vision. The participants were arranged into groups by type of chronic condition. T-test analysis was performed to determine significant differences between participants with and without each of the selected condition. If there was no difference between the selected chronic condition subgroup and the remaining participants with no such conditions, the participants were included in the study. This was the case for participants with systemic hypertension (henceforth referred to as hypertension) who rarely exhibit significant loss of spatial vision. Hypertension is common in the ageing population and exclusion of these participants would not represent the current status of the ageing population. For example in the Netherlands in 2010 31.4% of the population had hypertension (Blokstra et al., 2011). The

prevalence differs between males and females and increases with age. The percentages of males and females suffering from hypertension in the Netherlands in the fifth, sixth, seventh and eighth decade was found to be 27.8%, 47.4%, 61.8% ,70.7% and 14.7%, 31.5%, 55.3%, 69.3%, respectively (Blokstra et al., 2011). The results of more recent studies with a representative adult population in the north of the Netherlands were comparable (Klijs et al., 2015; van der Ende et al., 2017). Figure 4.6 shows the prevalence of hypertension in the Netherlands per 1000 people in 2019. These are the estimated numbers generally used by general practitioners (Nielen et al., 2020). Participants that were clinically diagnosed with diabetes were excluded since this systemic disease is known to affect several aspects of vision (Katz et al., 2010; Dosso et al., 1996; Della Sala et al., 1985; Abdel-Hay et al., 2018; O'Neill-Biba et al., 2010).

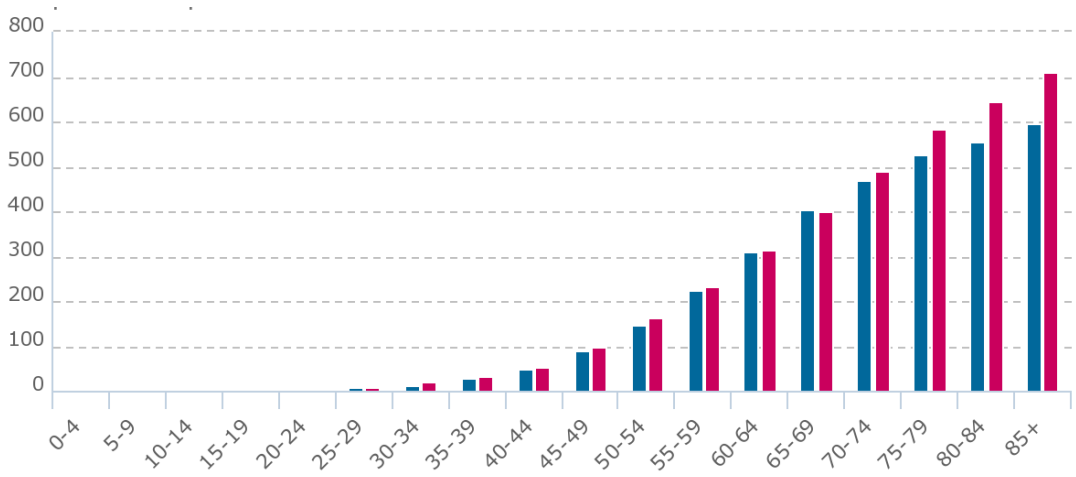


Figure 4.6 Prevalence of hypertension in the Netherlands in 2019 per age bin of 5 years. The blue bars represent men, and the pink bars women. (Nielen et al., 2020).

2. Absence of current signs of ocular disease, conventional or refractive laser surgery, corneal dystrophies or clear lens extraction. Participants with nuclear, cortical and posterior subcapsular lens opacities graded 3 or higher (according to the Optometry Grading Scale) were excluded (Pearson, 2003). The remaining participants were included in our sample simply because a grading of two or lower is very common in an ageing population and, as a result, one may be justified to attribute these smaller changes to ‘normal’ healthy ageing.

3. A new filter was developed and applied to detect those with subclinical, but yet unidentified visual problems. The filter relies on comparison of thresholds

measured with the same stimulus parameters in each of the two eyes. Since changes caused by either the optics of the eye or diseases of the retina rarely affect both eyes in exactly the same way (Brown and Yap, 1995; Toit, 1998), participants with abnormal differences of VA and/or FCS between the two eyes were not included in the analysis for normal age limits. The index employed to describe the Inter Ocular Difference (IOD) between the log values of the measured thresholds in the two eyes was, IOD = ABS(Log RE – Log LE). Figure 4.7 (A-D) and 4.8 (A-D) shows the statistical distribution of this parameter for VA and for FCS measurements respectively when using the photopic and mesopic protocol. All participants with threshold differences greater than 2.5σ units were classed as outliers and excluded from the analysis. Both VA and FCS measurements can be affected by changes in the lens and the optical media, more so than other visual functions such as colour vision. The 2.5σ was used, to ensure that few if any subjects with deviations from the mean threshold were excluded in the analysis.

4. In addition, the results for the remaining study participants were reanalysed per decade and all outliers with log thresholds outside the ±2.5σ range with respect to the corresponding mean threshold values were also removed from the analysis. This filter was applied separately to each measurement condition. At this last stage of screening for normal healthy vision, the study participants eliminated from the analysis varied from 0 to just under 2.5%, depending on the stimulus condition.

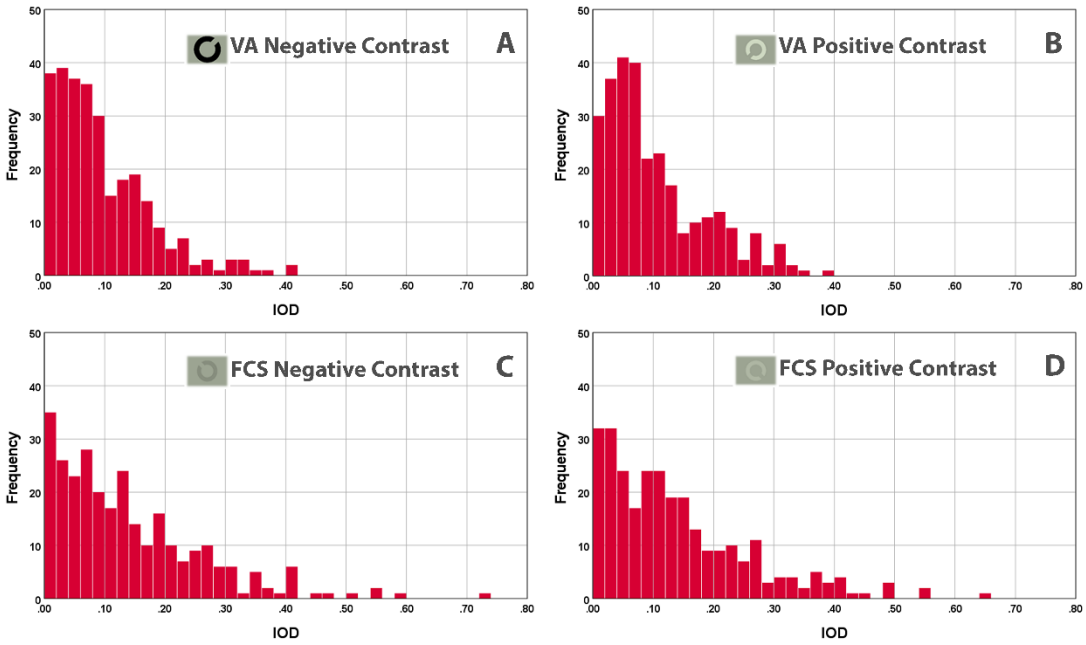


Figure 4.7 (A-D) Frequency histograms showing observed distributions of fractional differences between the two eyes for photopic VA measured with negative contrast (A) and positive contrast (B) and for photopic FCS measured with negative contrast (C) and positive contrast (D). The measured variables were converted to log units and the Inter Ocular Difference (IOD) is expressed as, IOD = ABS(T_{RE} – T_{LE}), where T_{RE} and T_{LE} represent the thresholds measured for each stimulus condition in the right and the left eyes in log units. The mean values for T_{RE} - T_{LE} are close to zero, but the use of absolute values for the differences in the measured thresholds in the two eyes doubles the number of measurements on one side of the histogram. Participants with absolute thresholds greater than 2.5σ are not included in the analysis.

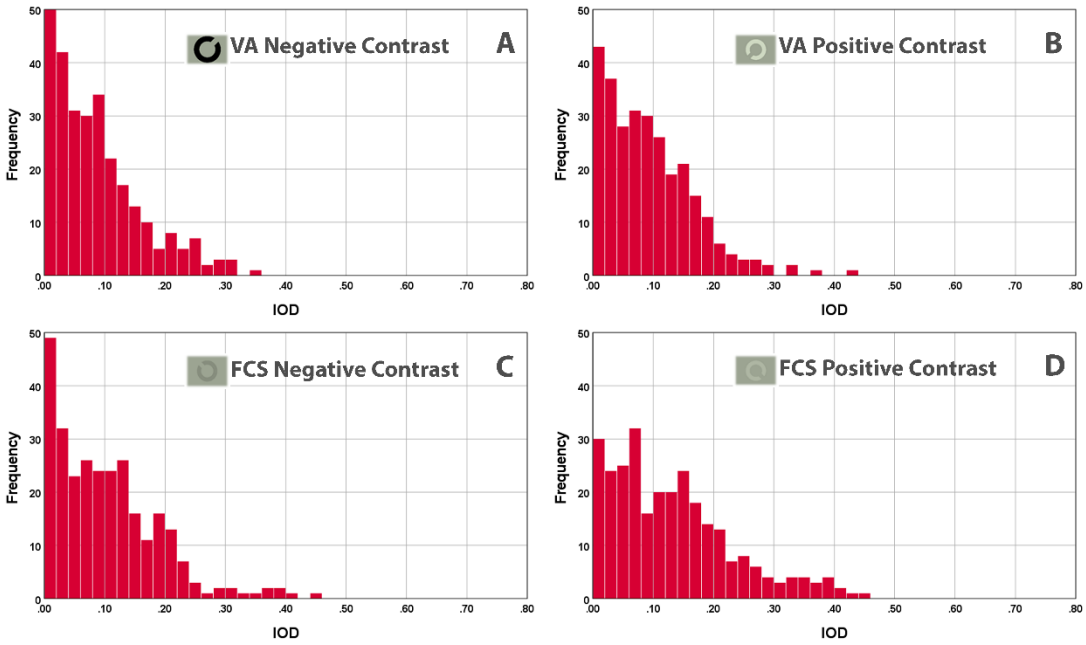


Figure 4.8 (A-D) Frequency histograms showing observed distributions of fractional differences between the two eyes for mesopic VA measured with negative contrast

(A) and positive contrast (B) and for mesopic FCS measured with negative contrast (C) and positive contrast (D). The measured variables were converted to log units and the Inter Ocular Difference (IOD) is expressed as, IOD = ABS($T_{RE} – T_{LE}$), where T_{RE} and T_{LE} represent the thresholds measured for each stimulus condition in the right and the left eyes in log units. The mean values for T_{RE} - T_{LE} are close to zero, but the use of absolute values for the differences in the measured thresholds in the two eyes doubles the number of measurements on one side of the histogram. Participants with absolute thresholds greater than 2.5σ are not included in the analysis.

The literature is not consistent about identifying amblyopia, but most commonly amblyopia is considered to be present if there is a difference between the two eyes of at least two rows on an eye chart (Thompson et al., 1991; Kiorpes and McKee, 1999). Depending on the criteria used to identify amblyopia, prevalence is estimated from 0.2% to 5.3% of the population (Attebo et al., 1998). Participants with amblyopia were excluded based on medical history and a two-line difference between the two eyes on the eye chart. Additionally, participants with tropias and a lack of stereoacuity were not included. In the current study, it was important to identify participants with amblyopia to be excluded from the normal group. The reduction of unilateral or bilateral (less common) best corrected VA in amblyopia is not a result of structural abnormality in the eye. The origin is not optical or organic (Kiorpes and McKee, 1999). A positive diagnostic test for amblyopia is not available and the diagnosis is based on exclusion of uncorrected refractive error and underlying ocular pathology in patients with a condition such as strabismus and anisometropia.

4.6 Statistical Analysis

Statistical analyses were carried out using SPSS (version 25, Chicago, Illinois, USA) and JMP (version 14, Marlow, Buckinghamshire, UK). Figures were made in Excel (version 2016, Microsoft, Redmond, Washington, USA) and SPSS. In SPSS, characteristics of participants were reported as distributions and frequencies for categorical variables in each decade. Shapiro-Wilk tests were conducted as normality tests. In general, when adequate sample sizes were available, the data were normally distributed and parametric tests perform well (Minitab, 2015a; Minitab, 2015b; Minitab, 2015c). The selected filters identified those participants who performed spatial vision tasks within normal statistical limits for the corresponding age. Paired samples t-tests were used to compare within and between eye differences, and a one-way ANOVA was conducted to compare the photopic and mesopic measurements between the different test locations. Independent t-tests were conducted to compute differences between subsequent

decades. All statistical comparisons carried out employed Bonferroni correction to account for multiple comparisons. The adjusted alpha levels for statistical significance following Bonferroni correction varied depending on the analysis involved, largely because the number of comparisons varied between 3 and 12. With Bonferroni the critical alpha level (0.05) is divided by the number of comparisons made. For example, 12 comparisons result in a Bonferroni corrected alpha level of 0.004. Correlations between the two polarities and between VA and FCS thresholds were analysed by Pearson correlation coefficient. Differences between negative and positive contrast results were presented in a Bland-Altman plot. The Bland-Altman plots were produced with the calculated limits of agreements (LoAs) and their confidence intervals (CIs). The CIs are important to estimate the reliability of the LoAs, and were calculated by the exact two-sided tolerance approach (Bunce, 2009; Carkeet, 2020; Carkeet, 2015). In specific samples the LoAs may vary from the limits based on the population (Carkeet, 2015). Simple linear regressions were conducted to predict FCS based upon VA in participants with normal mesopic visual performance. All the monocular analyses were performed with the right or left eye, determined by randomisation. Some of the comparisons were also conducted with the right and left eye data separately, to provide insight in the differences between randomised and non-randomised analyses.

The participants were initially separated into decades during recruitment and analysis. The ageing trend based on visual estimation was minimal within decades and the statistical estimates based on the number of participants examined between decades were more accurate because of larger sample sizes. This approach is in agreement with other studies (Elliott and Whitaker, 1992; Puell et al., 2004b; Mäntyjärvi and Laitinen, 2001) on the effect of age on visual functions. Fitting non-linear functions to mean and ±2.5σ limits produced better results with smaller range limits for the best fit parameters when more points were involved. Preliminary tests also confirmed that the Gauss-Newton method for fitting non-linear functions works best when a larger number of points is involved. The number of points were therefore doubled to benefit the Gauss-Newton, non-linear, curve fitting method by using five year bins. The calculated threshold limits for each subgroup correspond to the mean, mean +2.5σ (Upper Normal Limit, UNL) and mean -2.5σ (Lower Normal Limit, LNL).

A model with biologically meaningful parameters was fitted to the data to predict lower normal limit, mean and upper normal limit functions for each of the 16 data

sets. The 16 data sets which consisted of 8 photopic and 8 mesopic are listed in table 4.2.

Photopic	Mesopic
VA Negative Contrast Monocular	VA Negative Contrast Monocular
VA Negative Contrast Binocular	VA Negative Contrast Binocular
VA Positive Contrast Monocular	VA Positive Contrast Monocular
VA Positive Contrast Binocular	VA Positive Contrast Binocular
FCS Negative Contrast Monocular	FCS Negative Contrast Monocular
FCS Negative Contrast Binocular	FCS Negative Contrast Binocular
FCS Positive Contrast Monocular	FCS Positive Contrast Monocular
FCS Positive Contrast Binocular	FCS Positive Contrast Binocular

Table 4.2 Listing of the 16 data sets obtained in this study. Lower normal limits, medians and upper normal limits were computed for each set separately.

The optimization of best fit model parameters to each data set was carried out using the Gauss-Newton method in JMP. Preliminary examination of the data helped with the selection of the starting values for the model parameters. Thresholds were stable or increased minimally in the first few decades, but exhibited a more rapid increase in both median values as well as inter-subject variability above 50 years of age in photopic condition and above 30 years of age in mesopic condition. The following, four parameter, non-linear model was fitted to each of the 16 sets of data investigated:

$$\text{Dependent variable} = b_1 + b_2 * \{\text{Exp}\,(\text{Age} - b_3)^{b4} - 1\} \qquad \text{Eq. 1}$$

This data inspired model allows us to attach some meaning to describe the observed characteristics of normal healthy ageing of spatial vision:

- b_1 is largely determined by the upper horizontal asymptote when age has little, if any effect, on the measured thresholds,
- b_2 is a weighting factor that applies to every age, but only affects the results significantly when the participant's age is greater than b_3.
- b_3 is an important parameter which determines the age above which the exponential function starts affecting the measured thresholds and is followed by a more rapid increase in threshold with increasing age.
- Finally, parameter, b_4, controls the speed of exponential growth in thresholds with advancing age.

The fitted curves are plotted as a function of age together with the measured thresholds for each of the study participants.

5. Results

This chapter describes the obtained results. First the study population and the effect of the different filters are outlined. Of the participants included after the various filters, within and between comparisons and correlations are documented. The chapter ends with the effect of ageing, and the determination of age-related normal limits of VA and FCS thresholds, subsequently for photopic and mesopic conditions.

5.1 Study population

382 Caucasian participants were included. These participants were divided into 15 groups based on their self-reported medical history and ocular abnormalities as diagnosed upon examination. Table 5.1 shows an overview of the different groups. Less common systemic and ocular conditions were combined in the other systemic conditions group, and the other ocular conditions group, respectively, whereas relatively common fundus anomalies were categorised into the fundus abnormalities group. The other systemic conditions group consisted of participants with hypothyroidism, hyperthyroidism, epilepsy, attention deficit hyperactivity disorder (ADHD), collitus ulcerosa, cardiovascular disease and multiple sclerosis. Keratoconus (n=1) and multifocal intraocular lens implantation (n=2) were categorised into the other ocular conditions group. Participants with the following fundus abnormalities were included in the fundus anomaly group: AMD, Best vitelliform macular dystrophy, hyper- and hypo pigmented macula, glaucomatous optic neuropathy (henceforth referred to as glaucoma), history of retinal detachment surgery, Roth spots, macular exudates (star) and oedema, past history of central serous retinopathy and macular pucker. The largest group, the healthy group, consisted of 243 individuals who had no self-reported systemic conditions and ocular abnormalities found during a comprehensive eye examination. The second largest group was the hypertensive group with 42 participants. Hypertension was well controlled in all participants and none had any signs of hypertensive retinopathy. Independent t- tests were performed to calculate the differences in all 12 Acuity-*Plus* test measurements between the healthy participants and the participants with hypertension. The tests were conducted for each decade separately, except for the first and second decade as these decades did not include participants with hypertension.

Group	n	Male / Female	Age (years; M ± SD)
Healthy	243	95 / 148	40.53 ± 18.84
Hypertension	42	20 / 22	65.40 ± 10.22
Diabetes	3	1 / 2	64.50 ± 3.47
Diabetes and Hypertension	6	1 / 5	70.78 ± 7.68
Hyperlipidaemia	7	2 / 5	63.57 ± 6.48
Rheumatoid Arthritis	5	1 / 4	50.00 ± 20.87
Allergic Rhinitis	3	0 / 3	37.70 ± 8.06
Asthma	4	0 / 4	46.08 ± 23.86
Other systemic conditions	18	7 / 11	56.30 ± 19.49
Amblyopia	16	4 / 12	49.84 ± 19.90
Fundus Abnormalities	18	8 / 10	62.64 ± 12.57
Congenital Lens Opacities	2	1 / 1	18.90 ± 3.68
Other ocular conditions	3	0 / 3	53.23 ± 6.96
Refractive Laser Surgery	10	1 / 9	43.58 ± 8.39
Ortho K Lenses	2	1 / 1	26.05 ± 17.04
Total	**382**	**142 / 240**	**46.68 ± 19.85**

Table 5.1 Overview of participants included in the current research based on their medical history and ocular abnormalities. Abbreviations: n = number; M = mean; SD = standard deviation.

Independent t-tests revealed no statistically significant differences for any of the photopic and mesopic VA and FCS measurements between participants with hypertension and age-matched healthy participants ($P>0.05$). These findings demonstrate that visual performance did not differ between the two groups. Based on these results, the group of participants with hypertension was added to the healthy group for further analyses. Furthermore, inclusion of hypertensive participants in the normal group also represents the current status of the ageing population (Klijs et al., 2015; van der Ende et al., 2017; Blokstra et al., 2011).
The participants with other systemic or ocular conditions were not compared with the healthy group as the number of these participants per decade were small. None of them were included in the calculations of normal age-related limits as these conditions may influence photopic and/or mesopic VA and FCS. However, a graphical presentation of the performance of the groups with systemic or ocular abnormalities compared to the established age-related normal limits, is shown in figures 7.1 (A-D) to 7.10 (A-D).
Adding the hypertension group to the healthy group, resulted in a total of 285 participants. Two filters were applied to exclude outliers within this group. First, the

participants with an IOD above 2.5 sigma in one or more measurements were identified and excluded (n = 27). The filter relies on comparison of thresholds measured with the same stimulus parameters in each of the two eyes. Since changes caused by either the optics of the eye or diseases of the retina rarely affect both eyes in exactly the same way, participants with abnormal differences of VA and/or FCS between the two eyes were not included in the analysis of normal age limits (Brown and Yap, 1995; Toit, 1998). After this filter, the normal visual performance group consisted of 258 participants and the mean and standard deviation were calculated for each decade of life. In a second step, filters were applied individually for each measurement. Participants with thresholds above 2.5 sigma were excluded from the specific condition. This filter was employed for each condition separately to account for the effects of the optics of the eye, such as higher-order aberrations and the expected loss of retinal sensitivity to contrast in the mesopic range (Patterson, Bargary and Barbur, 2015).

As a result of applying the filters described above, the study involved between 252 and 258 participants depending on the stimulus condition employed. The effects of each filter on the final outcome are shown graphically in figure 5.1. Table 5.2 shows the characteristics of the participants with normal visual performance included before the filter per condition was applied. Both healthy participants and those with hypertension were included in the normal vision group. The sample included more female than male participants (n=155; 60.1% vs n=103; 39.9%). The mean age of the healthy group is lower in comparison to the group with hypertension. This is not surprising given that the prevalence of hypertension is higher in the elderly (van der Ende et al., 2017; Klijs et al., 2015). The majority of participants did not smoke and had no previous history of smoking (n=191; 74%). Some participants were smokers (n=16; 6.2%) or had previously been a smoker (n=51; 19.8%). In the normal photopic vision group, eyes with myopic spherical equivalent refractive error were more common (n=285; 55.2%) than hyperopic refractive error (n=143; 27.7%) and emmetropia (n=88; 17.1%). On cover test, most of the participants demonstrated orthophoria (n=210; 81.4%) for distance, followed by exophoria (n=26; 10.1%) and esophoria (n=22; 8.5%). The cover test is important in evaluating binocular vision and of interest in the analysis of binocular summation. Opacification of the lens, measured using the Optometry Grading Scale (Pearson, 2003) were found to be more common in the nucleus of the lens. The mean gradings following the Optometry Grading Scale for nuclear-, cortical- and posterior subcapsular cataract were respectively 1.00, 0.04 and 0.02 for the right eye, and 1.00, 0.03 and 0.02 for the left eye. These mean values could be interpreted as low as the severity of the

cataracts with this grading scale ranges from 1 to 5, with 1 indicating mild cataracts and 5 indicating dense cataracts.

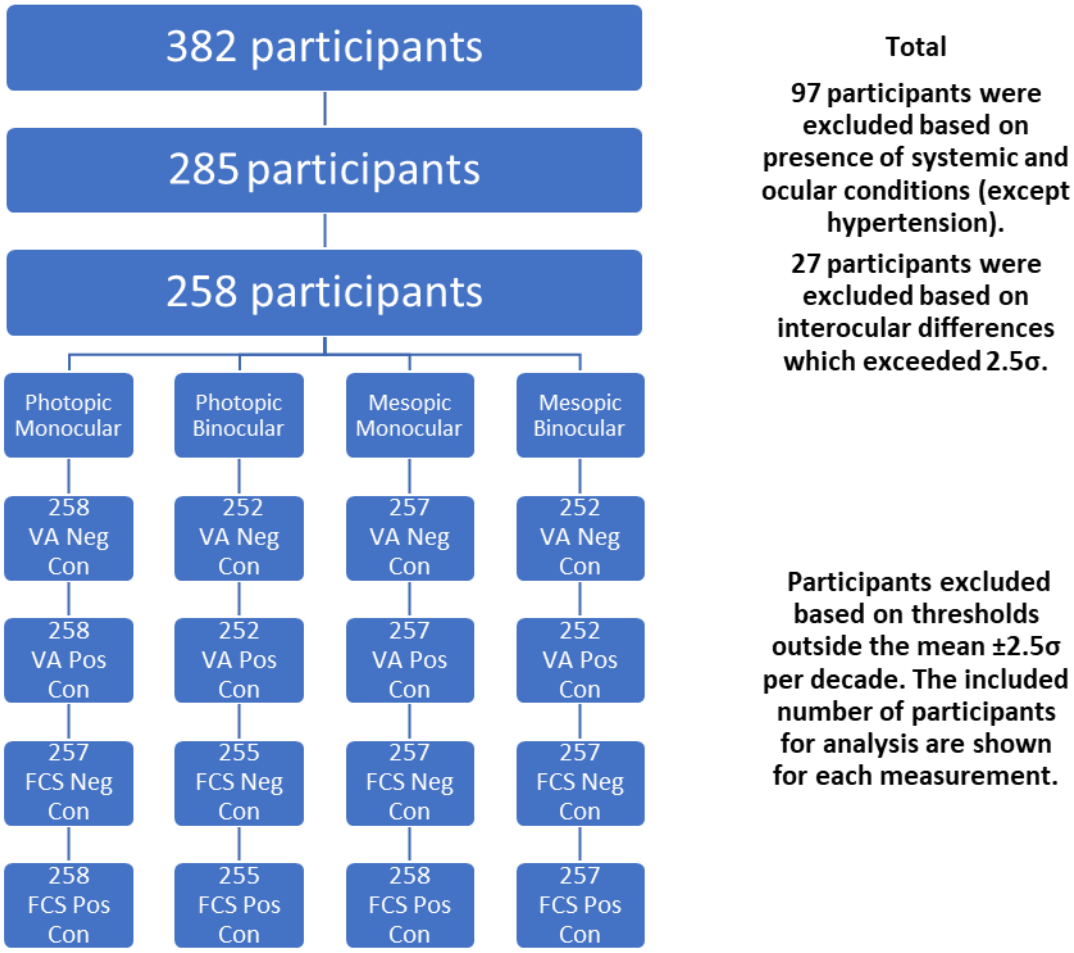


Figure 5.1 Flowchart shows the number of participants who failed each of the filtering criteria employed in the study. The very small differences in the final sample sizes are caused by applying the 2.5σ filter separately to each of the 16 stimulus conditions. Abbreviations: VA = visual acuity; FCS = functional contrast sensitivity; Neg = negative; Pos = positive; Con = contrast.

	Healthy group (n=222)	Hypertension group (n=36)	Total normal visual performance group (n=258)
Age (years)	**M ± SD**	**M ± SD**	**M ± SD**
	40.11 ± 18.39	63.86 ± 9.85	43.40 ± 19.30
Gender	**n (%)**	**n (%)**	**n (%)**
Male	87 (39.2)	16 (44.4)	103 (39.3)
Female	135 (60.8)	20 (55.6)	155 (60.1)
Smoking status	**n (%)**	**n (%)**	**n (%)**
Current	12 (5.4)	4 (11.1)	16 (6.2)
Former	41 (18.5)	10 (27.8)	51 (19.8)
Never	169 (76.1)	22 (61.1)	191 (74)
Spherical Equivalent Refractive Error	**n (%)**	**n (%)**	**n (%)**
Right eye			
Myopic	125 (56.3)	19 (52.8)	144 (55.8)
Hyperopic	38 (17.1)	13 (36.1)	72 (27.9)
Emmetropic	59 (26.6)	4 (11.1)	42 (16.3)
Left Eye			
Myopic	121 (54.5)	20 (55.6)	141 (54.7)
Hyperopic	59 (26.6)	12 (33.3)	71 (27.5)
Emmetropic	42 (18.9)	4 (11.1)	46 (17.8)
Ocular Lens Opacities according to the Optometry Grading Scale	**M ± SD**	**M ± SD**	**M ± SD**
Right eye			
Cortical M ± SD	0.02 ± 0.15	0.16 ± 0.63	0.04 ± 0.26
Nuclear M ± SD	0.89 ± 0.82	1.75 ± 0.44	1.00 ± 0.83
Posterior Subcapsular M ± SD	0.02 ± 0.16	0.03 ± 0.18	0.02 ± 0.17
Left Eye			
Cortical M ± SD	0.02 ± 0.13	0.09 ± 0.53	0.03 ± 0.23
Nuclear M ± SD	0.89 ± 0.82	1.78 ± 0.42	1.00 ± 0.83
Posterior Subcapsular M ± SD	0.01 ± 0.12	0.03 ± 0.18	0.02 ± 0.13
ETDRS Photopic Visual Acuity	**M logMAR ± SD** ***(M in MOA)***	**M logMAR ± SD** ***(M in MOA)***	**M logMAR ± SD** ***(M in MOA)***
BCVA Right Eye	-0.09 ± 0.09 *(0.81)*	-0.07 ± 0.10 *(0.85)*	-0.09 ± 0.09 *(0.81)*
BCVA Left Eye	-0.09 ± 0.09 *(0.81)*	-0.08 ± 0.08 *(0.83)*	-0.09 ± 0.09 *(0.81)*
BCVA Binocular	-0.15 ± 0.08 *(0.71)*	-0.13 ± 0.08 *(0.93)*	-0.15 ± 0.08 *(0.71)*

Table 5.2 (Continued)

	Healthy group (n=222)	Hypertension group (n=36)	Total normal visual performance group (n=258)
Acuity *Plus* test photopic VA	**M logMAR ± SD *(M in MOA)***	**M logMAR ± SD *(M in MOA)***	**M logMAR ± SD *(M in MOA)***
Photopic VA Neg Contrast Right Eye	0.07 ± 0.14 *(1.18)*	0.16 ± 0.14 *(1.45)*	0.08 ± 0.14 *(1.20)*
Photopic VA Neg Contrast Left Eye	0.06 ± 0.14 *(1.15)*	0.13 ± 0.14 *(1.35)*	0.07 ± 0.14 *(1.18)*
Photopic VA Neg Contrast Binocular	-0.03 ± 0.13 *(0.93)*	0.06 ± 0.12 *(1.15)*	-0.02 ± 0.13 *(0.96)*
Photopic VA Pos Contrast Right Eye	0.10 ± 0.14 *(1.26)*	0.20 ± 0.14 *(1.59)*	0.12 ± 0.14 *(1.38)*
Photopic VA Pos Contrast Left Eye	0.09 ± 0.13 *(1.23)*	0.16 ± 0.12 *(1.45)*	0.10 ± 0.13 *(1.26)*
Photopic VA Pos Contrast Binocular	0.00 ± 0.12 *(1.00)*	0.09 ± 0.11 *(1.23)*	0.02 ± 0.13 *(1.05)*
Acuity *Plus* test photopic FCS	**M log (%) ± SD *(M in %)***	**M log (%) ± SD *(M in %)***	**M log (%) ± SD *(M in %)***
Photopic FCS Neg Contrast Right Eye	1.16 ± 0.22 *(14.45)*	1.32 ± 0.23 *(20.89)*	1.18 ± 0.23 *(15.14)*
Photopic FCS Neg Contrast Left Eye	1.16 ± 0.22 *(14.45)*	1.31 ± 0.23 *(20.89)*	1.18 ± 0.22 *(15.14)*
Photopic FCS Neg Contrast Binocular	1.00 ± 0.21 *(10.00)*	1.18 ± 0.21 *(15.14)*	1.03 ± 0.22 *(10.72)*
Photopic FCS Pos Contrast Right Eye	1.23 ± 0.22 *(16.98)*	1.39 ± 0.23 *(24.55)*	1.25 ± 0.22 *(17.78)*
Photopic FCS Pos Contrast Left Eye	1.23 ± 0.21 *(16.98)*	1.39 ± 0.21 *(24.55)*	1.25 ± 0.22 *(17.78)*
Photopic FCS Pos Contrast Binocular	1.05 ± 0.20 *(11.22)*	1.23 ± 0.22 *(16.98)*	1.08 ± 0.21 *(10.02)*
Acuity *Plus* test mesopic VA	**M logMAR ± SD *(M in MOA)***	**M logMAR ± SD *(M in MOA)***	**M logMAR ± SD *(M in MOA)***
Mesopic VA Neg Contrast Right Eye	0.31 ± 0.15 *(2.04)*	0.44 ± 0.15 *(2.75)*	0.33 ± 0.16 *(2.14)*
Mesopic VA Neg Contrast Left Eye	0.30 ± 0.15 *(2.00)*	0.41 ± 0.14 *(2.57)*	0.31 ± 0.15 *(2.04)*
Mesopic VA Neg Contrast Binocular	0.21 ± 0.13 *(1.62)*	0.33 ± 0.15 *(2.14)*	0.23 ± 0.14 *(1.70)*
Mesopic VA Pos Contrast Right Eye	0.37 ± 0.15 *(2.34)*	0.48 ± 0.15 *(3.02)*	0.39 ± 0.15 *(2.46)*
Mesopic VA Pos Contrast Left Eye	0.37 ± 0.14 *(2.34)*	0.48 ± 0.15 *(3.02)*	0.39 ± 0.15 *(2.46)*
Mesopic VA Pos Contrast Binocular	0.26 ± 0.14 *(1.82)*	0.38 ± 0.15 *(2.40)*	0.28 ± 0.15 *(1.91)*
Acuity *Plus* test mesopic FCS	**M log (%) ± SD *(M in %)***	**M log (%) ± SD *(M in %)***	**M log (%) ± SD *(M in %)***
Mesopic FCS Neg Contrast Right Eye	1.68 ± 0.19 *(47.86)*	1.86 ± 0.13 *(72.44)*	1.71 ± 0.20 *(51.29)*
Mesopic FCS Neg Contrast Left Eye	1.67 ± 0.20 *(46.77)*	1.83 ± 0.15 *(67.61)*	1.69 ± 0.20 *(48.98)*
Mesopic FCS Neg Contrast Binocular	1.51 ± 0.21 *(32.36)*	1.74 ± 0.18 *(54.95)*	1.54 ± 0.22 *(34.67)*
Mesopic FCS Pos Contrast Right Eye	1.78 ± 0.21 *(60.26)*	1.94 ± 0.17 *(87.10)*	1.80 ± 0.21 *(63.10)*
Mesopic FCS Pos Contrast Left Eye	1.76 ± 0.20 *(57.54)*	1.92 ± 0.17 *(83.18)*	1.78 ± 0.21 *(60.26)*
Mesopic FCS Pos Contrast Binocular	1.59 ± 0.22 *(38.91)*	1.82 ± 0.20 *(66.07)*	1.62 ± 0.23 *(41.69)*

Table 5.2 Participant characteristics in the normal visual performance group before the filter per condition was applied. Abbreviations: n = number, M = mean; SD = standard deviation; ETDRS = Early Treatment Diabetic Retinopathy Study; VA = visual acuity; FCS = functional contrast sensitivity; logMAR = logarithm of the minimum angle of resolution; log = logarithm; MOA = minutes of arc.

Figures 5.2 show the distribution of the participants per decade in the normal visual performance group before the filter per condition was applied.

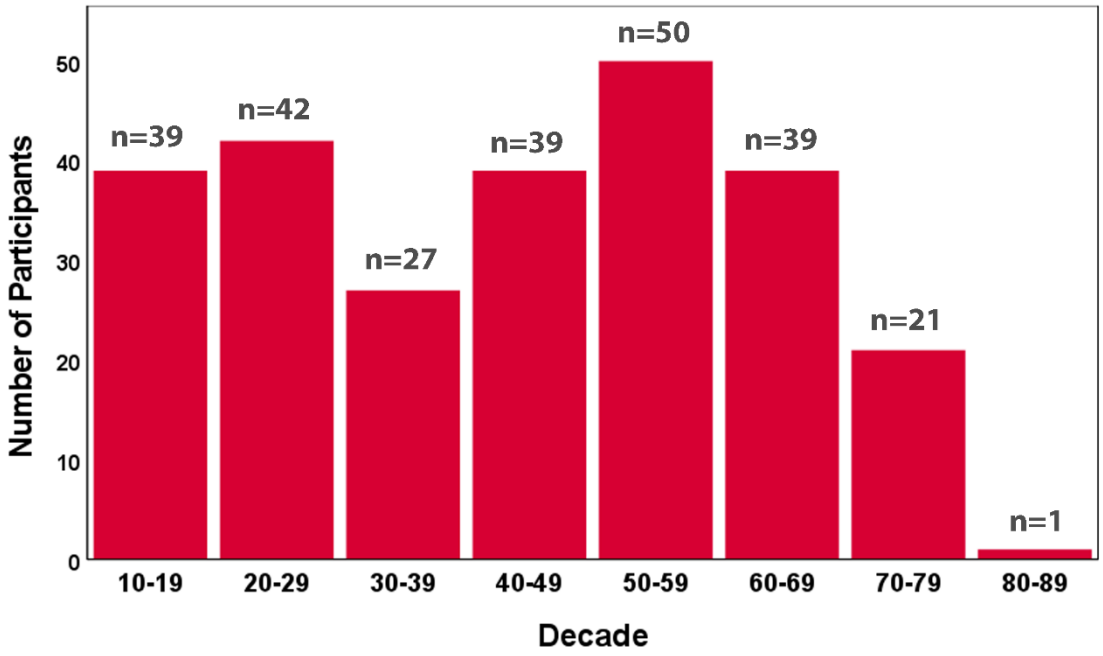


Figure 5.2 Distribution of participants in the normal visual performance group before the filter per condition was applied (n=258).

5.2 Within and between participants comparisons of the photopic conditions in the normal vision group

Differences between male and female photopic VA and FCS Acuity-*Plus* test results were analysed with an independent t- test. All paired tests were performed with the binocular, left eye, the right eye and the left and right eye randomised results. The only exceptions were the differences between the right and left eye and between the first and second eye tested. No significant differences were found between males and females for any of the photopic measurements ($P>0.004$). Paired t-tests were also conducted to compare negative and positive contrast Acuity-*Plus* test results, the right and left eye results, photopic negative contrast VA with Acuity-*Plus* test and ETDRS test results. Due to multiple testing Bonferroni corrections were applied. Paired t-tests showed significantly higher photopic positive contrast VA and FCS Acuity-*Plus* test thresholds compared to photopic negative contrast thresholds ($P<0.008$). Differences between the photopic right eye and left eye VA and FCS

results were not statistically significant (P>0.013). The order in which the two eyes were tested also showed no difference to the results for both VA and FCS (P>0.013). Photopic VA thresholds measured with negative contrast optotypes were compared against the equivalent ETDRS VA data. Paired t-tests revealed significant differences between the two tests with slightly larger VA thresholds measured with the Acuity-*Plus* test (P<0.017). The results are shown in table 5.3. To test for difference between testing sites, a one-way ANOVA was conducted for photopic measurements between the testing sites. Per decade, no statistically significant differences were found between groups for all photopic VA and FCS measurements (P>0.004).

Visual Acuity within eye difference	**M logMAR± SD** *(M MOA)*	**P**
Photopic negative contrast VA RE	0.08 ± 0.14 *(1.20)*	**<0.001***
Photopic positive contrast VA RE	0.12 ± 0.14 *(1.32)*	
Photopic negative contrast VA LE	0.07 ± 0.14 *(1.17)*	**<0.001***
Photopic positive contrast VA LE	0.10 ± 0.13 *(1.26)*	
Photopic negative contrast VA Binocular	-0.02 ± 0.13 *(0.95)*	**<0.001***
Photopic positive contrast VA Binocular	0.02 ± 0.13 *(1.05)*	
Photopic negative contrast VA Random	0.08 ± 0.15 *(1.20)*	**<0.001***
Photopic positive contrast VA Random	0.11 ± 0.14 *(1.29)*	
Functional Contrast Sensitivity within eye difference	**M log (%) ± SD** *(M in %)*	**P**
Photopic negative contrast FCS RE	1.18 ± 0.23 *(15.14)*	**<0.001***
Photopic positive contrast FCS RE	1.25 ± 0.22 *(17.78)*	
Photopic negative contrast FCS LE	1.18 ± 0.22 *(15.14)*	**<0.001***
Photopic positive contrast FCS LE	1.25 ± 0.22 *(17.78)*	
Photopic negative contrast FCS Binocular	1.03 ± 0.22 *(10.72)*	**<0.001***
Photopic positive contrast FCS Binocular	1.08 ± 0.21 *(12.02)*	
Photopic negative contrast FCS Random	1.19 ± 0.23 *(15.49)*	**<0.001***
Photopic positive contrast FCS Random	1.25 ± 0.23 *(17.78)*	
Visual Acuity between eye difference	**M logMAR± SD** *(M MOA)*	**P**
Photopic negative contrast VA RE	0.08 ± 0.14 *(1.20)*	0.057**
Photopic negative contrast VA LE	0.07 ± 0.14 *(1.17)*	
Photopic positive contrast VA RE	0.12 ± 0.14 *(1.32)*	0.022**
Photopic positive contrast VA LE	0.10 ± 0.13 *(1.26)*	
Functional Contrast Sensitivity between eye difference	**M log (%) ± SD** *(M in %)*	
Photopic negative contrast FCS RE	1.18 ± 0.23 *(15.14)*	0.945**
Photopic negative contrast FCS LE	1.18 ± 0.22 *(15.14)*	
Photopic positive contrast FCS RE	1.25 ± 0.22 *(17.78)*	0.930**
Photopic positive contrast FCS LE	1.25 ± 0.22 *(17.78)*	
Comparison VA measured with Acuity Plus test vs. EDTRS	**M logMAR± SD** *(M MOA)*	**P**
Photopic negative contrast VA RE	0.08 ± 0.14 *(1.20)*	**<0.001*****
ETDRS VA RE	-0.09 ± 0.09 *(0.81)*	
Photopic negative contrast VA LE	0.07 ± 0.14 *(1.17)*	**<0.001*****
ETDRS VA LE	-0.09 ± 0.09 *(0.81)*	
Photopic negative contrast VA Binocular	-0.02 ± 0.13 *(0.95)*	**<0.001*****
ETDRS VA Binocular	-0.15 ± 0.08 *(0.71)*	
Photopic negative contrast VA Random	0.08 ± 0.15 *(1.20)*	**<0.001*****
ETDRS VA Random	-0.09 ± 0.09 *(0.81)*	

Table 5.3 Comparison of photopic results within the normal vision group using paired t-tests.
Level of statistical significance adjusted for multiple testing: *= 0.008 **= 0.013 ***=0.017. Abbreviations: M = mean; SD = standard deviation; RE= right eye; LE= left eye; ETDRS = Early Treatment Diabetic Retinopathy Study; VA = visual acuity; FCS = functional contrast sensitivity; logMAR = logarithm of the minimum angle of resolution; log = logarithm; MOA = minutes of arc.

5.3 Correlations photopic conditions in normal vision group

Pearson correlation coefficients were calculated to assess the relationship between the photopic negative and positive contrast results. Monocular correlation analyses were performed with the right or left eye, determined by randomisation. There was a strong positive correlation between positive and negative contrast thresholds of the monocular (r = 0.805, R^2= 0.649, P<0.001, n=258) and binocular (r = 0.811, R^2= 0.657, P<0.001, n=258) photopic VA measurements. Pearson correlations between the negative and positive contrast thresholds were very strong for the monocular (r = 0.883, R^2= 0.780, P<0.001, n=258) and binocular (r = 0.876, R^2= 0.768, P<0.001, n=258) FCS measurements. Figure 5.3 (A-D) shows the Bland-Altman plots of differences between negative and positive contrast monocular and binocular photopic VA and FCS thresholds. For the monocular analyses, randomised right or left eye thresholds were used. The smaller the limits of agreement, the better the agreement between negative and positive contrast. Figure 5.3 (A-D) shows the datapoints representing the difference between two measurements to be symmetrically distributed about the mean difference, which indicated random variability.

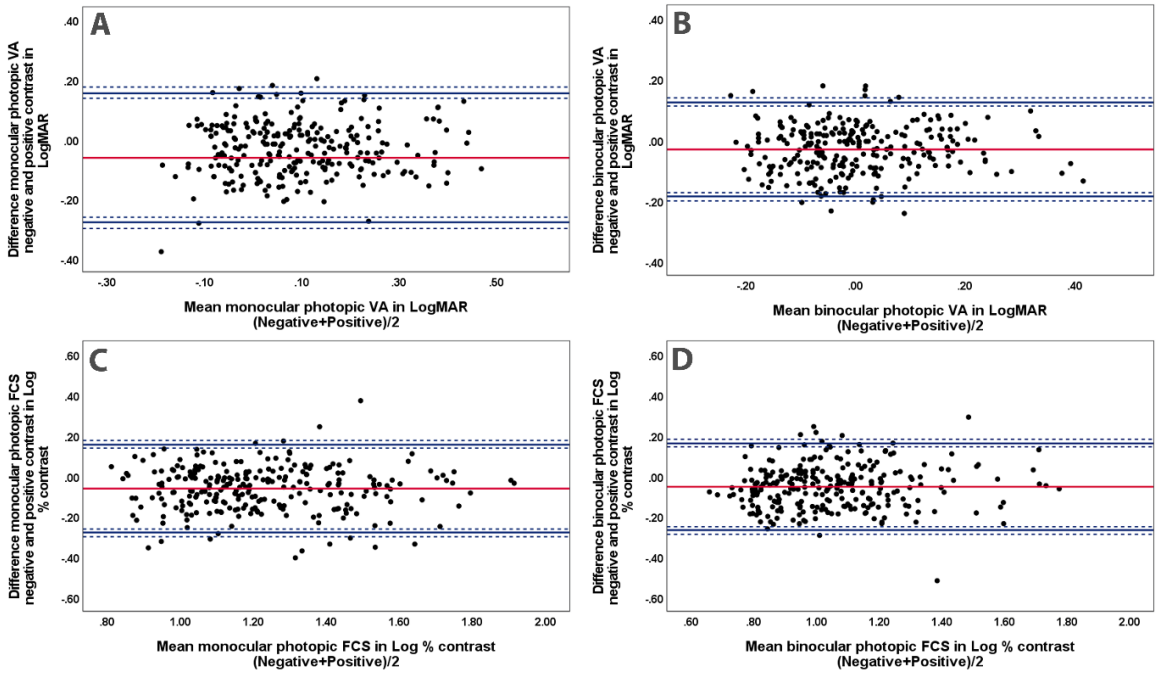


Figure 5.3 (A-D) Bland-Altman analysis between negative and positive contrast thresholds for photopic monocular VA (A), photopic binocular VA (B), photopic monocular FCS (C) and photopic binocular FCS (D). In each graph the red solid line represents the average of the difference, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

The graphs show better performance with negative contrast for all photopic measurements. The mean difference for monocular photopic VA was -0.03 logMAR (upper LoA, 95% CI: 0.143, 0.129 to 0.160; lower LoA, 95% CI: -0.209, -0.195 to -0.226), and for binocular VA was -0.03 logMAR (upper LoA, 95% CI: 0.124, 0.112 to 0.138; lower LoA, 95% CI: -0.185, -0.173 to -0.199). For the photopic FCS measurements, monocular mean difference was -0.06 log units (upper LoA, 95% CI: 0.155, 0.138 to 0.176; lower LoA, 95% CI: -0.278, -0.261 to -0.299), and binocular FCS mean difference was -0.05 log units (upper LoA, 95% CI: 0.161, 0.144 to 0.182; lower LoA, 95% CI: -0.266, -0.250 to -0.287). In addition, Pearson correlation coefficients were conducted to assess the relationship between the VA and FCS thresholds for both contrast polarities. A strong positive correlation between negative contrast VA and FCS thresholds with photopic monocular (r = 0.761, R^2=0.579, P<0.001, n=258) and binocular (r = 0.791, R^2=0.625, P<0.001, n=258) measurements was found. The positive contrast photopic VA and FCS results were strongly positive correlated, for both monocular (r = 0.762, R^2=0.581, P<0.001, n=258) and binocular (r = 0.798, R^2=0.636, P<0.001, n=258) measurements. Simple linear regression analyses were used to predict FCS based upon VA in participants with normal visual performance. The monocular analyses were performed with the right or left eye results, determined by randomisation. Linear regression equations exhibited a good prediction of photopic negative contrast monocular thresholds by VA (F= 351.67, P<0.001) with R^2 being 0.579 and binocular thresholds (F= 427.32, P<0.001) and R^2 being 0.625. Photopic positive contrast thresholds could also be well predicted by VA based on regression analysis of monocular (F= 355.34, P<0.001, R^2=0.581) and binocular (F= 447.41, P<0.001, R^2=0.636) results. The linear regression plots of the photopic measurements are shown in figure 5.4 (A-D).

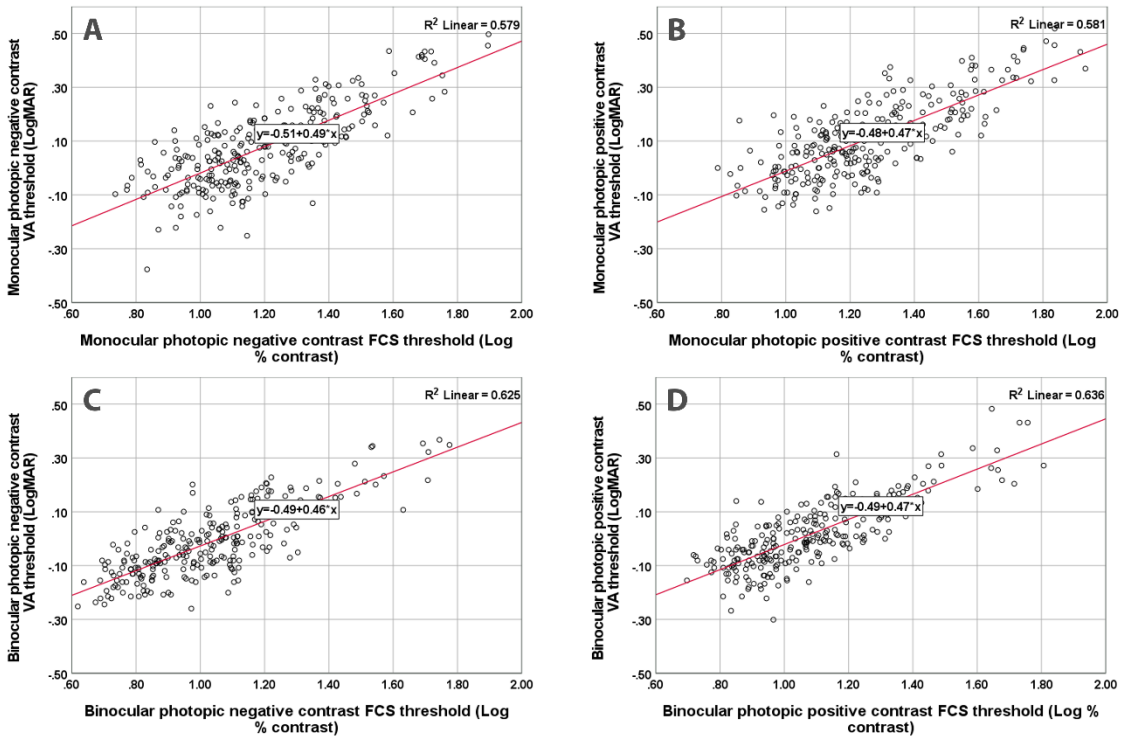


Figure 5.4 (A-D) Linear regression plots predicting photopic FCS thresholds by photopic VA thresholds for monocular negative contrast (A), monocular positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D).

5.4 Within and between participants comparisons of the mesopic conditions in the normal vision group

Except for the ETDRS results, the same comparisons as in photopic conditions were performed within the normal vision group for mesopic conditions (table 5.4). The ETDRS VA and mesopic negative contrast Acuity-*Plus* test VA comparisons were not conducted if the ETDRS VA was performed under photopic light conditions only. All analyses, except the differences between the two eyes, were performed with the binocular, right eye, left eye and randomised right or left eye results. Independent t-tests revealed no differences between males and females for any of the mesopic VA and FCS measurements (P>0.004). Mesopic negative contrast VA thresholds were significantly better than mesopic positive contrast thresholds when compared using a paired t-test (P<0.008). Comparison of the right and left eyes with the paired t-test revealed no significant differences between eyes in the mesopic conditions (P>0.013). The order in which the two eyes were tested made no difference to the results for both, VA and FCS (P>0.013). One-way ANOVA revealed no statistically significant differences per decade between testing sites for all mesopic VA and FCS measurements differences (P>0.004).

Visual Acuity within eye difference	**M logMAR± SD** ***(M MOA)***	**P**
Mesopic negative contrast VA RE	0.33 ± 0.16 *(2.14)*	**<0.001***
Mesopic positive contrast VA RE	0.39 ± 0.15 *(2.45)*	
Mesopic negative contrast VA LE	0.31 ± 0.15 *(2.04)*	**<0.001***
Mesopic positive contrast VA LE	0.39 ± 0.15 *(2.45)*	
Mesopic negative contrast VA Binocular	0.23 ± 0.14 *(1.70)*	**<0.001***
Mesopic positive contrast VA Binocular	0.28 ± 0.15 *(1.91)*	
Mesopic negative contrast VA Random	0.32 ± 0.16 *(2.09)*	**<0.001***
Mesopic positive contrast VA Random	0.38 ± 0.16 *(2.40)*	
Functional Contrast Sensitivity within eye difference	**M log (%) ± SD** ***(M in %)***	**P**
Mesopic negative contrast FCS RE	1.71 ± 0.20 *(51.29)*	**<0.001***
Mesopic positive contrast FCS RE	1.80 ± 0.21 *(63.10)*	
Mesopic negative contrast FCS LE	1.69 ± 0.20 *(48.98)*	**<0.001***
Mesopic positive contrast FCS LE	1.78 ± 0.21 *(60.26)*	
Mesopic negative contrast FCS Binocular	1.54 ± 0.22 *(34.67)*	**<0.001***
Mesopic positive contrast FCS Binocular	1.62 ± 0.23 *(41.69)*	
Mesopic negative contrast FCS Random	1.70 ± 0.20 *(50.12)*	**<0.001***
Mesopic positive contrast FCS Random	1.80 ± 0.22 *(63.10)*	
Visual Acuity between eye difference	**M logMAR± SD** ***(M MOA)***	**P**
Mesopic negative contrast VA RE	0.33 ± 0.16 *(2.14)*	0.021**
Mesopic negative contrast VA LE	0.31 ± 0.15 *(2.04)*	
Mesopic positive contrast VA RE	0.39 ± 0.15 *(2.45)*	0.878**
Mesopic positive contrast VA LE	0.39 ± 0.15 *(2.45)*	
Functional Contrast Sensitivity between eye difference	**M log (%) ± SD** ***(M in %)***	**P**
Mesopic negative contrast FCS RE	1.71 ± 0.20 *(51.29)*	0.018**
Mesopic negative contrast FCS LE	1.69 ± 0.20 *(48.98)*	
Mesopic positive contrast FCS RE	1.80 ± 0.21 *(63.10)*	**0.008****
Mesopic positive contrast FCS LE	1.78 ± 0.21 *(60.26)*	

Table 5.4 Comparison of mesopic results within the normal vision group using paired t-tests.
Level of statistical significance adjusted for multiple testing: *= 0.008 **= 0.013.
Abbreviations: M = mean; SD = standard deviation; RE= right eye; LE= left eye; ETDRS = Early Treatment Diabetic Retinopathy Study; VA = visual acuity; FCS = functional contrast sensitivity; logMAR = logarithm of the minimum angle of resolution; log = logarithm; MOA = minutes of arc.

5.5 Correlations mesopic conditions in normal vision group

Pearson correlation coefficients revealed very strong positive correlation between negative and positive contrast VA thresholds with monocular (r = 0.851, R^2=0.725, P<0.001, N=258) and binocular (r = 0.841, R^2=0.725, P<0.001, n=258) measurements. Monocular analyses were performed with right or left eye results, determined by randomisation. Pearson correlations between the negative and

positive mesopic FCS results were also very strong for the monocular (r = 0.876, R^2=0.767, P<0.001, n=258) and binocular (r = 0.864, R^2=0.746, P<0.001, n=258) measurements. The Bland-Altman plots of differences between negative and positive contrast of monocular and binocular mesopic VA and FCS thresholds are shown in figure 5.5 (A-D). The Bland-Altman plots shows better performance with negative contrast for all mesopic measurements. For mesopic VA measurements, monocular mean difference was -0.06 logMAR (upper LoA, 95% CI: 0.107, 0.09 to 0.123; lower LoA, 95% CI: -0.230, -0.217 to -0.246), and for binocular VA was -0.05 logMAR (upper LoA, 95% CI: 0.109, 0.096 to 0.124; lower LoA, 95% CI: -0.206, -0.194 to -0.221). The mean difference for mesopic monocular FCS was -0.09 log units (upper LoA, 95% CI: 0.112, 0.100 to 0.131; lower LoA, 95% CI: -0.298, -0.282 to -0.318), and binocular FCS was -0.08 log units (upper LoA, 95% CI: 0.152, 0.133 to 0.174; lower LoA, 95% CI: -0.317, -0.299 to -0.340). Overall, the points, which represent the difference between the thresholds of the two measurements, are symmetrically distributed, indicating that variability is random. An exception is the mesopic monocular FCS, which can be explained by the limited threshold of 2.00 log (100%) in negative contrast.

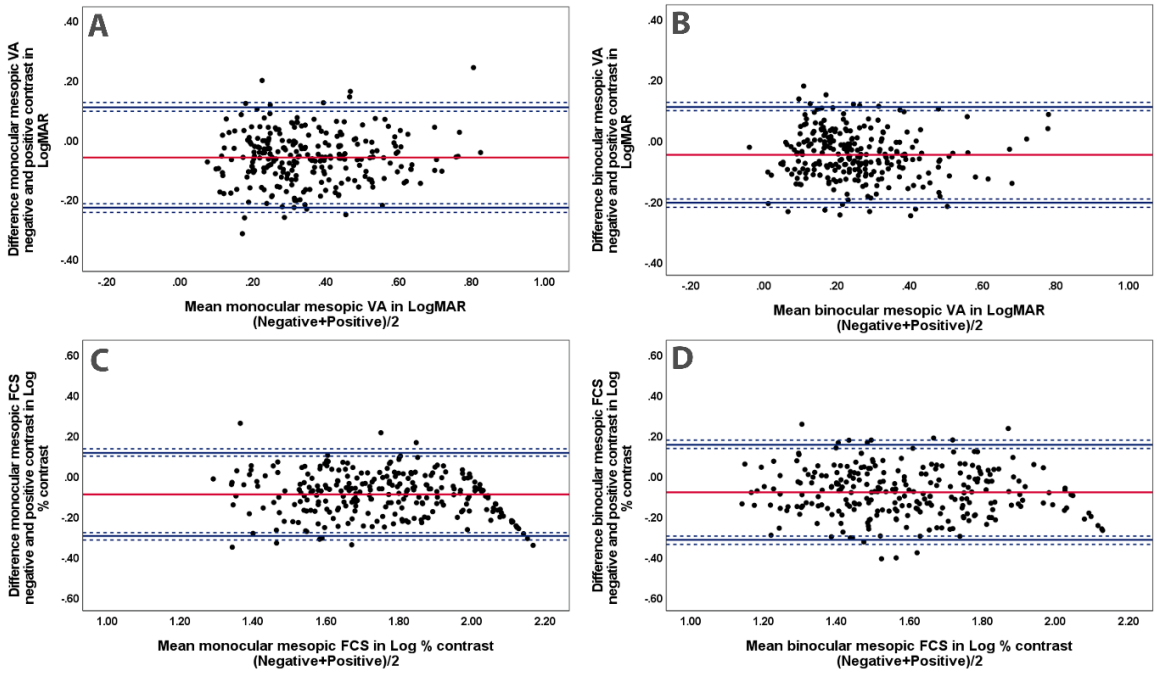


Figure 5.5 (A-D) Bland-Altman analysis between negative and positive contrast thresholds for mesopic monocular VA (A), mesopic binocular VA (B), mesopic monocular FCS (C) and mesopic binocular FCS (D). In each graph the red solid line represents the average of the differences, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

Due to the threshold limit, the mean monocular and binocular FCS thresholds are slightly skewed in the higher mean values (figure 5.5 C-D).

Correlations between mesopic VA and FCS results were calculated using the Pearson correlation coefficient. Between mesopic negative contrast VA and FCS thresholds, a very strong positive correlation was found for monocular (r = 0.831, R^2=0.690, P<0.001, n=258) and binocular (r = 0.834, R^2=0.695, P<0.001, n=258) results. A strong positive correlation between the mesopic positive contrast VA and FCS monocular (r = 0.851, R^2=0.725, P<0.001, n=258) and binocular (r = 0.831, R^2=0.690, P<0.001, n=258) thresholds was found. Simple linear regressions were conducted to predict FCS based upon VA in participants with normal visual performance. Prior to the monocular analyses the right and left eye were randomised to be included. Linear regression equations exhibited a good prediction of mesopic negative contrast monocular thresholds by VA (F= 569.33, P<0.001, R^2=0.690) and binocular thresholds (F= 584.43, P<0.001, R^2=0.695). Mesopic positive contrast thresholds could also be well predicted by VA based on regression analysis of monocular (F= 674.30, P<0.001, R^2=0.725) and binocular (F= 571.07, P<0.001, R^2=0.690) results. Figure 5.6 (A-D) shows the linear regression plots of the mesopic measurements.

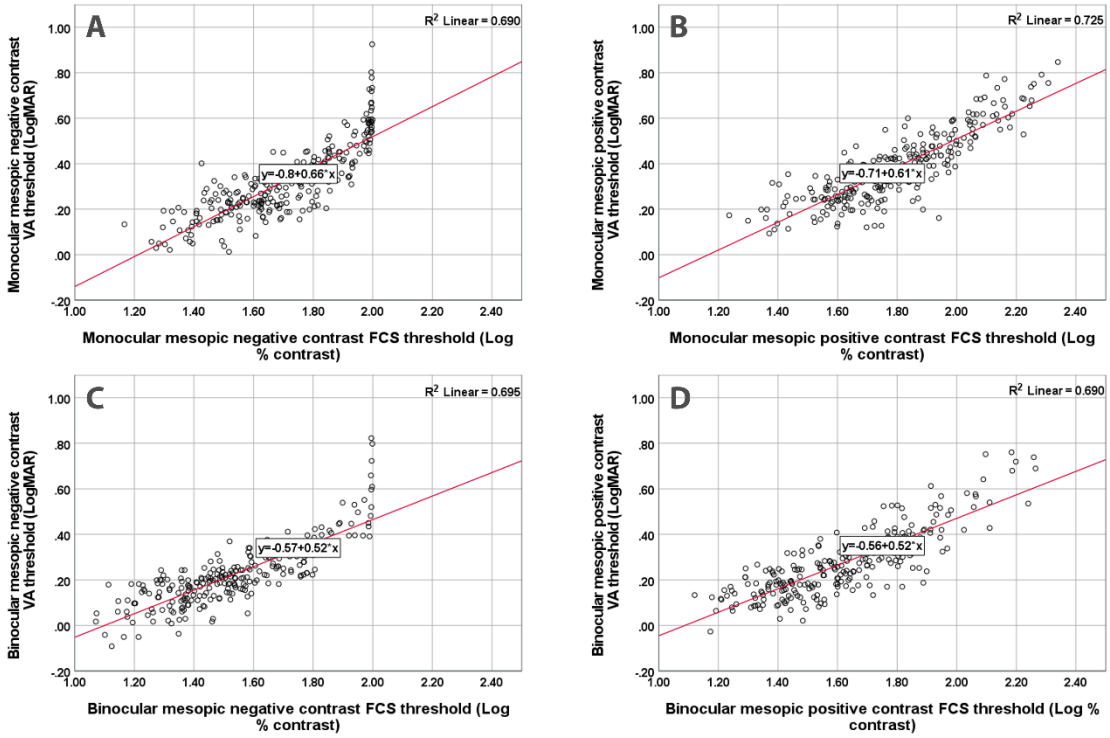


Figure 5.6 (A-D) Linear regression plots predicting mesopic FCS thresholds by mesopic VA thresholds of monocular negative contrast (A), monocular positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D).

5.6 The effect of ageing on Photopic Visual Acuity

Mean thresholds were calculated for each decade separately. The mean photopic VA thresholds in logMAR and standard deviations are shown in table 5.5. In addition, the mean is presented in minutes of arc. Independent t-tests were conducted to compare the mean thresholds for each decade with the threshold for each subsequent decade. A Bonferroni correction was applied due to multiple testing. Statistically significant differences (P<0.004) were found in comparisons above the fifth decade: specifically, between the fifth and sixth decade for negative contrast VA for the right and positive contrast VA for the right eye. Differences were statistically significant between the sixth and seventh decade for positive contrast binocular VA (P<0.004). The randomised monocular results (right or left eye) showed a significant difference between the sixth and the seventh decade for positive contrast VA (P<0.004).

	10-19 year	20-29 year	30-39 year	40-49 year	50-59 year	60-69 year	70-79 year	80-89 year
	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	logMAR *(MOA)*
N	39	41	26	39	48	39	21	1
Photopic negative contrast VA RE	0.02 ± 0.12 *(1.05)*	0.01 ± 0.10 *(1.02)*	0.04 ± 0.09 *(1.10)*	0.02 ± 0.13 *(1.05)*	0.09 ± 0.10 *(1.23)*	0.17 ± 0.12 *(1.48)*	0.19 ± 0.16 *(1.55)*	0.45 *(2.82)*
N	39	42	26	39	49	38	21	1
Photopic negative contrast VA LE	0.00 ± 0.10 *(1.00)*	-0.01 ± 0.12 *(0.98)*	0.02 ± 0.13 *(1.05)*	0.05 ± 0.12 *(1.12)*	0.10 ± 0.13 *(1.26)*	0.14 ± 0.10 *(1.38)*	0.17 ± 0.12 *(1.48)*	0.35 *(2.24)*
N	38	41	26	39	48	38	21	1
Photopic negative contrast VA Binocular	-0.10 ± 0.09 *(0.79)*	-0.09 ± 0.08 *(0.81)*	-0.07 ± 0.10 *(0.85)*	-0.04 ± 0.11 *(0.91)*	0.00 ± 0.10 *(1.00)*	0.07 ± 0.09 *(1.17)*	0.11 ± 0.13 *(1.35)*	0.20 *(1.58)*
N	39	42	27	39	50	39	21	1
Photopic negative contrast VA Random	0.01 ± 0.11 *(1.02)*	0.01 ± 0.11 *(1.02)*	0.03 ± 0.16 *(1.07)*	0.03 ± 0.13 *(1.07)*	0.11 ± 0.13 *(1.29)*	0.16 ± 0.12 *(1.45)*	0.20 ± 0.16 *(1.58)*	0.45 *(2.82)*
N	38	41	27	38	49	39	21	1
Photopic positive contrast VA RE	0.04 ± 0.11 *(1.10)*	0.04 ± 0.10 *(1.10)*	0.08 ± 0.14 *(1.20)*	0.07 ± 0.11 *(1.17)*	0.15 ± 0.11 *(1.41)*	0.22 ± 0.11 *(1.66)*	0.21 ± 0.16 *(1.62)*	0.43 *(2.69)*
N	39	42	27	38	50	38	21	1
Photopic positive contrast VA LE	0.04 ± 0.09 *(1.10)*	0.05 ± 0.11 *(1.12)*	0.04 ± 0.11 *(1.10)*	0.06 ± 0.10 *(1.15)*	0.13 ± 0.13 *(1.35)*	0.20 ± 0.10 *(1.58)*	0.18 ± 0.10 *(1.51)*	0.37 *(2.34)*
N	38	41	26	38	49	38	21	1
Photopic positive contrast VA Binocular	-0.06 ± 0.08 *(0.87)*	-0.05 ± 0.09 *(0.89)*	-0.04 ± 0.08 *(0.91)*	-0.02 ± 0.10 *(0.95)*	0.03 ± 0.10 *(1.07)*	0.10 ± 0.08 *(1.26)*	0.15 ± 0.13 *(1.41)*	0.27 *(1.86)*
N	39	42	27	39	50	39	21	1
Photopic positive contrast VA Random	0.04 ± 0.11 *(1.10)*	0.03 ± 0.11 *(1.07)*	0.07 ± 0.13 *(1.17)*	0.07 ± 0.12 *(1.17)*	0.14 ± 0.13 *(1.38)*	0.23 ± 0.10 *(1.70)*	0.20 ± 0.15 *(1.58)*	0.43 *(2.69)*

Table 5.5 Mean photopic VA thresholds in logMAR, standard deviation and mean in minutes of arc per decade. Abbreviations: M = mean; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity; MOA = minutes of arc; RE = right eye; LE = left eye.

	10-14 year	**15-19 year**	**20-24 year**	**25-29 year**	**30-34 year**	**35-39 year**	**40-44 year**	**45-49 year**	**50-54 year**	**55-59 year**	**60-64 year**	**65-69 year**	**70-74 year**	**75-79 year**	**80-84 year**
	M logMAR ± SD ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**logMAR** ***(MOA)***
N	22	17	17	24	18	8	19	20	27	21	22	17	14	7	1
Photopic negative contrast VA RE	0.02 ± 0.14 *(1.05)*	0.02 ± 0.14 *(1.05)*	-0.01 ± 0.10 *(0.98)*	0.03 ± 0.10 *(1.07)*	0.02 ± 0.08 *(1.05)*	0.07 ± 0.12 *(1.17)*	0.03 ± 0.13 *(1.07)*	0.01 ± 0.13 *(1.02)*	0.09 ± 0.11 *(1.23)*	0.11 ± 0.09 *(1.29)*	0.14 ± 0.14 *(1.38)*	0.20 ± 0.07 *(1.58)*	0.17 ± 0.15 *(1.48)*	0.21 ± 0.20 *(1.62)*	0.45 *(2.82)*
N	22	17	17	25	18	8	19	20	27	22	21	17	14	7	1
Photopic negative contrast VA LE	0.00 ± 0.12 *(1.00)*	-0.01 ± 0.08 *(0.98)*	0.00 ± 0.13 *(1.00)*	-0.01 ± 0.11 *(0.98)*	0.02 ± 0.14 *(1.05)*	0.01 ± 0.12 *(1.02)*	0.07 ± 0.13 *(1.17)*	0.02 ± 0.12 *(1.05)*	0.09 ± 0.12 *(1.23)*	0.11 ± 0.14 *(1.29)*	0.14 ± 0.10 *(1.38)*	0.15 ± 0.09 *(1.41)*	0.16 ± 0.12 *(1.45)*	0.20 ± 0.12 *(1.58)*	0.35 *(2.24)*
N	21	17	16	25	18	8	19	20	27	21	21	17	14	7	1
Photopic negative contrast VA Binocular	-0.09 ± 0.11 *(0.81)*	-0.10 ± 0.07 *(0.79)*	-0.08 ± 0.06 *(0.83)*	-0.09 ± 0.09 *(0.81)*	-0.08 ± 0.10 *(0.83)*	-0.05 ± 0.10 *(0.89)*	-0.04 ± 0.10 *(0.91)*	-0.05 ± 0.11 *(0.89)*	-0.02 ± 0.10 *(0.95)*	0.02 ± 0.09 *(1.05)*	0.07 ± 0.10 *(1.17)*	0.08 ± 0.09 *(1.20)*	0.08 ± 0.11 *(1.20)*	0.16 ± 0.16 *(1.45)*	0.20 *(1.58)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Photopic negative contrast VA Random	-0.01 ± 0.13 *(0.98)*	0.03 ± 0.09 *(1.07)*	-0.03 ± 0.11 *(0.93)*	0.03 ± 0.11 *(1.07)*	0.03 ± 0.18 *(1.07)*	0.03 ± 0.11 *(1.07)*	0.04 ± 0.15 *(1.10)*	0.03 ± 0.12 *(1.07)*	0.10 ± 0.14 *(1.26)*	0.13 ± 0.13 *(1.35)*	0.17 ± 0.12 *(1.48)*	0.16 ± 0.11 *(1.45)*	0.17 ± 0.16 *(1.48)*	0.25 ± 0.16 *(1.78)*	0.45 *(2.82)*

Table 5.6 (Continued)

	10-14 year	**15-19 year**	**20-24 year**	**25-29 year**	**30-34 year**	**35-39 year**	**40-44 year**	**45-49 year**	**50-54 year**	**55-59 year**	**60-64 year**	**65-69 year**	**70-74 year**	**75-79 year**	**80-84 year**
	M logMAR ± SD ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**logMAR** ***(MOA)***
N	21	17	17	24	19	8	18	20	27	22	22	17	14	7	1
Photopic positive contrast VA RE	0.05 ± 0.11 *(1.12)*	0.02 ± 0.11 *(1.05)*	0.02 ± 0.11 *(1.05)*	0.05 ± 0.09 *(1.12)*	0.09 ± 0.14 *(1.23)*	0.06 ± 0.16 *(1.15)*	0.05 ± 0.11 *(1.12)*	0.08 ± 0.11 *(1.20)*	0.14 ± 0.11 *(1.38)*	0.17 ± 0.12 *(1.48)*	0.21 ± 0.11 *(1.62)*	0.24 ± 0.11 *(1.74)*	0.19 ± 0.16 *(1.55)*	0.25 ± 0.17 *(1.78)*	0.43 *(2.69)*
N	22	17	17	25	19	8	19	19	28	22	21	17	14	7	1
Photopic positive contrast VA LE	0.06 ± 0.10 *(1.15)*	0.01 ± 0.08 *(1.02)*	0.04 ± 0.10 *(1.10)*	0.06 ± 0.12 *(1.15)*	0.04 ± 0.13 *(1.10)*	0.05 ± 0.09 *(1.12)*	0.07 ± 0.11 *(1.17)*	0.05 ± 0.09 *(1.12)*	0.13 ± 0.13 *(1.35)*	0.13 ± 0.14 *(1.35)*	0.20 ± 0.11 *(1.58)*	0.20 ± 0.08 *(1.58)*	0.19 ± 0.10 *(1.55)*	0.17 ± 0.11 *(1.48)*	0.37 *(2.34)*
N	21	17	17	24	18	8	18	20	27	22	21	17	14	7	1
Photopic positive contrast VA Binocular	-0.04 ± 0.08 *(0.91)*	-0.08 ± 0.08 *(0.83)*	-0.05 ± 0.11 *(0.89)*	-0.05 ± 0.08 *(0.89)*	-0.05 ± 0.08 *(0.89)*	-0.02 ± 0.09 *(0.95)*	-0.02 ± 0.09 *(0.95)*	-0.01 ± 0.11 *(0.98)*	0.01 ± 0.10 *(1.02)*	0.04 ± 0.10 *(1.10)*	0.10 ± 0.09 *(1.26)*	0.11 ± 0.08 *(1.29)*	0.13 ± 0.10 *(1.35)*	0.19 ± 0.18 *(1.55)*	0.27 *(1.86)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Photopic positive contrast VA Random	0.06 ± 0.13 *(1.15)*	0.01 ± 0.09 *(1.02)*	0.01 ± 0.11 *(1.02)*	0.04 ± 0.11 *(1.10)*	0.07 ± 0.14 *(1.17)*	0.06 ± 0.12 *(1.15)*	0.06 ± 0.15 *(1.15)*	0.08 ± 0.18 *(1.20)*	0.13 ± 0.12 *(1.35)*	0.16 ± 0.14 *(1.45)*	0.24 ± 0.10 *(1.74)*	0.21 ± 0.11 *(1.62)*	0.21 ± 0.16 *(1.62)*	0.18 ± 0.13 *(1.51)*	0.43 *(2.69)*

Table 5.6 Mean photopic VA thresholds in logMAR, standard deviation and mean in minutes of arc per age bin of 5 years. Abbreviations: M = mean; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity; MOA = minutes of arc; RE = right eye; LE = left eye.

The analysis of the large data set aimed to produce mean, upper and lower normal limits as a function of age for the 16 test conditions. The measured data for the majority of the tests carried out were normally distributed, and this allowed us to use mean values and parametric tests for within and inter-participant comparisons. Some results, particularly those measured in older participants, produced more skewed distributions with few but clear outliers despite the filtering conditions designed to screen for normal healthy visual performance. To overcome this challenge and also the observed increased variability with increasing age, the data points were split into 5-years bins and mean and ±2.5σ calculated for each bin. Table 5.6 shows the mean values for each five-year age bin in logMAR and minutes of arc. The non-linear Gauss-Newton model was then fitted to each set of data points to predict each measurement's lower normal limit, mean and upper normal limit curves. The best-fit model parameters in table 5.7 describe means, upper and lower normal limits as a function of age. Figure 5.7 (A-D) displays the VA thresholds for each study participant measured in photopic conditions investigated in this study. In addition, figure 5.7 (A-D) also plots the predictions of the model for the mean VA and FCS thresholds as a function of age, together with the corresponding predictions for upper and lower normal threshold limits. The best-fit model parameters included in each graph describe means, upper and lower normal limits as a function of age. Mean photopic VA thresholds and age variability can be described as being largely age-invariant below 50 years of age. Above 50 years, both the mean thresholds and the observed inter-participant variability increases (figure 5.7 (A-D)). As expected, binocular results show lower VA thresholds and are less sensitive to inter-participant variability.

		b1	b2	b3	b4
Monocular Photopic VA Negative Contrast	M	0.074604703	0.1187083754	51	0.0309144395
	UNL	0.3585442924	0.0996937321	51	0.0410161286
	LNL	-0.211974179	0,1366666377	51	0,0232650189
Monocular Photopic VA Positive Contrast	M	0.1163477565	0.1536281499	51	0.0242149
	UNL	0.3987681032	0.171828971	51	0.0254339056
	LNL	-0.166339376	0.1334506025	51	0.022992706
Binocular Photopic VA Negative Contrast	M	-0.015666378	0.1295869895	51	0.0305986654
	UNL	0.226083817	0.1465884884	51	0.0342153535
	LNL	-0.258579034	0.1061126492	51	0.0271360741
Binocular Photopic VA Positive Contrast	M	0.0131516537	0.1046732918	51	0.0368765408
	UNL	0.2420119208	0.107671535	51	0.0446338656
	LNL	-0.219032931	0.0899875738	51	0.031262985

Table 5.7 Parameters of the Gauss-Newton formula for each photopic VA measurement. Abbreviations: VA = visual acuity; M = mean; UNL = upper normal limit; LNL = lower normal limit.

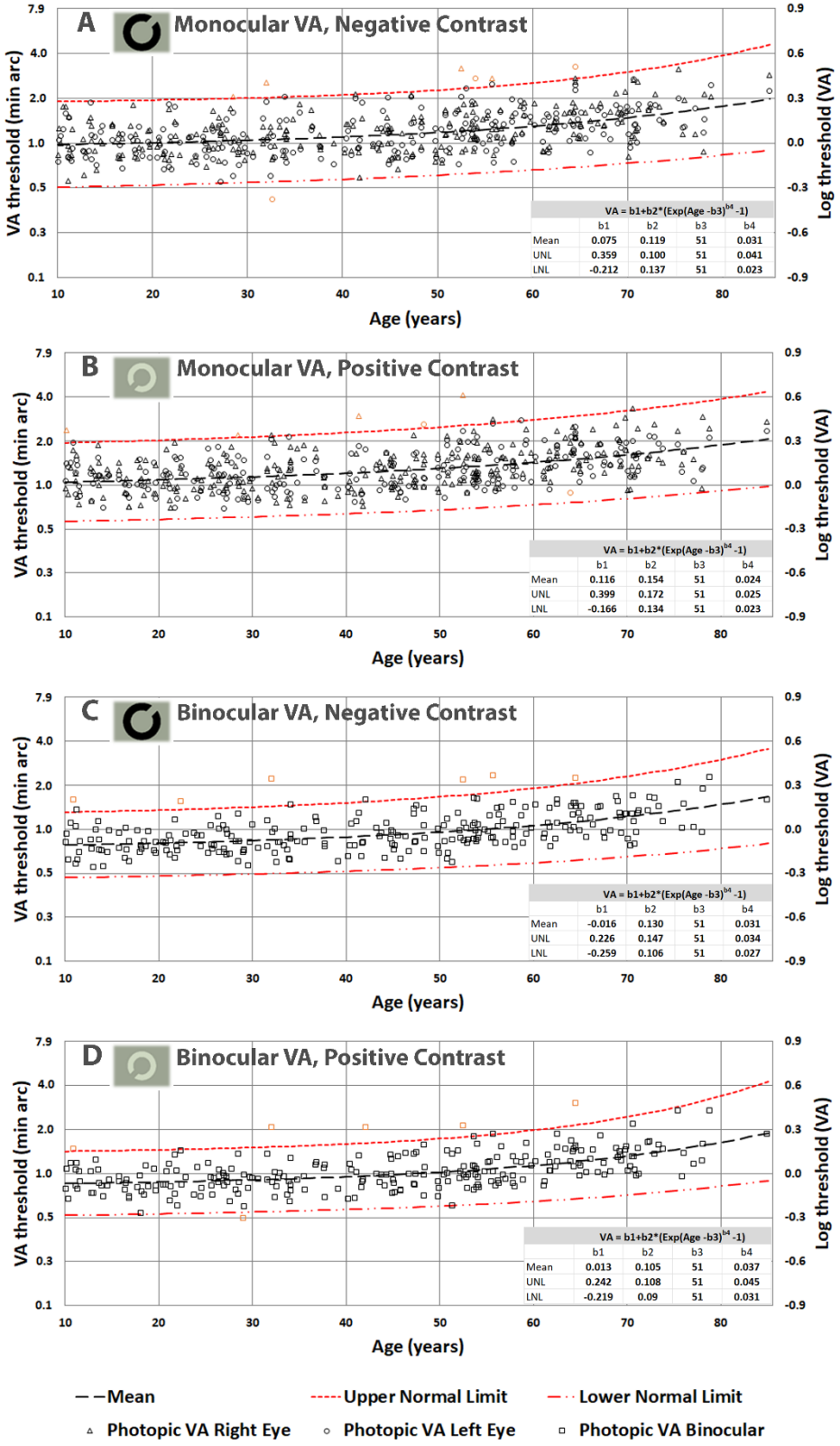


Figure 5.7 (A-D) Photopic VA thresholds in logMAR units and the corresponding minutes of arc plotted as a function of age; monocular (right and left eye data) negative contrast (A), monocular (right and left eye data) positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D). The inset for each stimulus condition lists the parameters needed to predict the fitted functions (i.e., Dependent variable = b1 + b2* {Exp (Age – b3)b4 -1}.

5.7 The effect of ageing on Mesopic Visual Acuity

Mesopic VA thresholds of each decade were also compared to the thresholds for each subsequent decade. Table 5.8 shows the mean mesopic VA thresholds in minutes of arc per decade, standard deviations and mean VA thresholds in logMAR. Independent t-tests revealed no significant differences up to the fifth decade. The comparisons between binocular negative contrast VA and binocular positive contrast VA were statistically significant (P<0.004) between the fifth and sixth decade. The other significant difference was found between the sixth and seventh decade for negative contrast VA of the right eye (P<0.004). The randomised monocular results showed significant differences between the fifth and sixth decade for positive contrast VA (P<0.004) and between the sixth and seventh decade for negative contrast VA(P<0.004). As described earlier, mean values and parametric tests for within and inter-participant comparisons were allowed if a majority of the results were normally distributed. However, particularly for mesopic conditions and in older participants, distributions were more skewed with few outliers, despite the filtering conditions designed to screen for normal healthy visual performance. For that reason, the data points were divided in 5 year bins, and non-linear functions fitted to each set of data points to predict mesopic VA measurement's lower normal limit, mean and upper normal limit curves. Mean values computed within each five-year bin are shown in logMAR and minutes of arc in table 5.9. The parameters of the model in table 5.10 describe means, upper and lower normal limits as a function of age. Figure 5.8 (A-D) displays the VA thresholds for each study participant measured in mesopic conditions investigated in this study. The predictions of the model for the mean mesopic VA and the corresponding upper and lower normal thresholds limits are also plotted in figure 5.8 (A-D). In addition, the best-fit model parameters included in each graph describe means, upper and lower normal limits as a function of age. Compared with the photopic VA results, mesopic VA starts with much larger values (e.g., parameter b1 in the fitted model) and the thresholds start to increase more rapidly above 30 years of age, particularly for positive contrast optotypes. An increase of inter-participant variability accompanies this. In comparison with the photopic VA results, mesopic VA thresholds are lower and show less pronounced increasing variability with age than the monocular results.

	10-19 year	20-29 year	30-39 year	40-49 year	50-59 year	60-69 year	70-79 year	80-89 year
	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	M logMAR ± SD *(M MOA)*	logMAR *(MOA)*
N	38	41	25	38	49	39	20	1
Mesopic negative contrast VA RE	0.22 ± 0.10 *(1.66)*	0.23 ± 0.11 *(1.70)*	0.26 ± 0.09 *(1.82)*	0.30 ± 0.11 *(2.00)*	0.35 ± 0.12 *(2.24)*	0.45 ± 0.11 *(2.82)*	0.49 ± 0.15 *(3.09)*	0.72 *(5.25)*
N	38	41	27	38	48	39	21	1
Mesopic negative contrast VA LE	0.23 ± 0.10 *(1.70)*	0.22 ± 0.12 *(1.66)*	0.24 ± 0.12 *(1.74)*	0.28 ± 0.09 *(1.91)*	0.33 ± 0.12 *(2.14)*	0.42 ± 0.12 *(2.63)*	0.48 ± 0.14 *(3.02)*	0.67 *(4.68)*
N	38	40	27	39	48	38	21	1
Mesopic negative contrast VA Binocular	0.13 ± 0.08 *(1.35)*	0.16 ± 0.08 *(1.45)*	0.18 ± 0.09 *(1.51)*	0.17 ± 0.09 *(1.48)*	0.25 ± 0.10 *(1.78)*	0.31 ± 0.08 *(2.04)*	0.41 ± 0.18 *(2.57)*	0.50 *(3.16)*
N	39	42	27	39	50	39	21	1
Mesopic negative contrast VA Random	0.23 ± 0.10 *(1.70)*	0.23 ± 0.13 *(1.70)*	0.25 ± 0.13 *(1.78)*	0.29 ± 0.09 *(1.95)*	0.36 ± 0.14 *(2.29)*	0.45 ± 0.12 *(2.82)*	0.51 ± 0.18 *(3.24)*	0.72 *(5.25)*
N	38	41	25	38	49	39	21	1
Mesopic positive contrast VA RE	0.27 ± 0.11 *(1.86)*	0.29 ± 0.11 *(1.95)*	0.32 ± 0.08 *(2.09)*	0.35 ± 0.11 *(2.24)*	0.42 ± 0.13 *(2.63)*	0.49 ± 0.12 *(3.09)*	0.54 ± 0.14 *(3.47)*	0.68 *(4.79)*
N	39	42	27	38	49	39	21	1
Mesopic positive contrast VA LE	0.28 ± 0.10 *(1.91)*	0.33 ± 0.13 *(2.14)*	0.31 ± 0.10 *(2.04)*	0.33 ± 0.11 *(2.14)*	0.42 ± 0.13 *(2.63)*	0.50 ± 0.13 *(3.16)*	0.53 ± 0.13 *(3.39)*	0.66 *(4.57)*
N	38	40	26	39	48	39	21	1
Mesopic positive contrast VA Binocular	0.19 ± 0.09 *(1.55)*	0.19 ± 0.08 *(1.55)*	0.21 ± 0.10 *(1.62)*	0.22 ± 0.09 *(1.66)*	0.31 ± 0.12 *(2.04)*	0.39 ± 0.10 *(2.45)*	0.43 ± 0.17 *(2.69)*	0.54 *(3.47)*
N	39	42	27	39	50	39	21	1
Mesopic positive contrast VA Random	0.27 ± 0.11 *(1.86)*	0.31 ± 0.13 *(2.04)*	0.33 ± 0.09 *(2.14)*	0.33 ± 0.12 *(2.14)*	0.43 ± 0.15 *(2.69)*	0.51 ± 0.12 *(3.24)*	0.56 ± 0.15 *(3.63)*	0.68 *(4.79)*

Table 5.8 Mean mesopic VA thresholds in logMAR, standard deviation and mean in minutes of arc per decade. Abbreviations: M = mean; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity; MOA = minutes of arc; RE = right eye; LE = left eye.

	10-14 year	**15-19 year**	**20-24 year**	**25-29 year**	**30-34 year**	**35-39 year**	**40-44 year**	**45-49 year**	**50-54 year**	**55-59 year**	**60-64 year**	**65-69 year**	**70-74 year**	**75-79 year**	**80-84 year**
	M logMAR ± SD ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**logMAR** ***(MOA)***
N	21	17	17	24	18	7	18	19	27	22	22	17	14	6	1
Mesopic negative contrast VA RE	0.24 ± 0.09 *(1.74)*	*0.19* ± *0.11* *(1.55)*	*0.24* ± *0.13* *(1.74)*	0.23 ± 0.11 *(1.70)*	0.23 ± 0.09 *(1.70)*	0.32 ± 0.09 *(2.09)*	0.33 ± 0.11 *(2.14)*	0.27 ± 0.11 *(1.86)*	0.35 ± 0.10 *(2.24)*	0.36 ± 0.14 *(2.29)*	0.43 ± 0.10 *(2.69)*	0.47 ± 0.11 *(2.95)*	0.50 ± 0.17 *(3.16)*	0.47 ± 0.13 *(2.95)*	0.72 *(5.25)*
N	21	17	17	24	19	8	18	20	27	21	22	17	14	7	1
Mesopic negative contrast VA LE	0.24 ± 0.10 *(1.74)*	0.21 ± 0.09 *(1.62)*	0.21 ± 0.14 *(1.62)*	0.22 ± 0.10 *(1.66)*	0.20 ± 0.10 *(1.58)*	0.31 ± 0.12 *(2.04)*	0.30 ± 0.10 *(2.00)*	0.27 ± 0.09 *(1.86)*	0.32 ± 0.12 *(2.09)*	0.34 ± 0.12 *(2.19)*	0.44 ± 0.12 *(2.75)*	0.41 ± 0.12 *(2.57)*	0.45 ± 0.13 *(2.82)*	0.53 ± 0.14 *(3.39)*	0.67 *(4.68)*
N	21	17	15	25	19	8	19	20	27	21	21	17	14	7	1
Mesopic negative contrast VA Binocular	0.12 ± 0.09 *(1.32)*	0.13 ± 0.07 *(1.35)*	0.15 ± 0.09 *(1.41)*	0.17 ± 0.08 *(1.48)*	0.16 ± 0.10 *(1.45)*	0.22 ± 0.06 *(1.66)*	0.18 ± 0.09 *(1.51)*	0.16 ± 0.10 *(1.45)*	0.25 ± 0.09 *(1.78)*	0.26 ± 0.11 *(1.82)*	0.31 ± 0.09 *(2.04)*	0.31 ± 0.06 *(2.04)*	0.40 ± 0.18 *(2.51)*	0.43 ± 0.20 *(2.69)*	0.50 *(3.16)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Mesopic negative contrast VA Random	0.26 ± 0.10 *(1.82)*	0.19 ± 0.09 *(1.55)*	0.21 ± 0.14 *(1.62)*	0.24 ± 0.13 *(1.74)*	0.22 ± 0.13 *(1.66)*	0.33 ± 0.12 *(2.14)*	0.31 ± 0.09 *(2.04)*	0.28 ± 0.10 *(1.91)*	0.33 ± 0.14 *(2.14)*	0.38 ± 0.14 *(2.40)*	0.47 ± 0.11 *(2.95)*	0.42 ± 0.14 *(2.63)*	0.48 ± 0.16 *(3.02)*	0.57 ± 0.20 *(3.72)*	0.72 *(5.25)*

Table 5.9 (Continued)

	10-14 year	**15-19 year**	**20-24 year**	**25-29 year**	**30-34 year**	**35-39 year**	**40-44 year**	**45-49 year**	**50-54 year**	**55-59 year**	**60-64 year**	**65-69 year**	**70-74 year**	**75-79 year**	**80-84 year**
	M logMAR ± SD ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**M logMAR ± SD** ***(M MOA)***	**logMAR** ***(MOA)***
N	22	16	17	24	18	7	18	20	27	22	22	17	14	7	1
Mesopic positive contrast VA RE	0.29 ± 0.12 *(1.95)*	0.24 ± 0.10 *(1.74)*	0.31 ± 0.13 *(2.04)*	0.27 ± 0.10 *(1.86)*	0.31 ± 0.08 *(2.04)*	0.36 ± 0.06 *(2.29)*	0.37 ± 0.10 *(2.34)*	0.33 ± 0.11 *(2.14)*	0.42 ± 0.11 *(2.63)*	0.43 ± 0.15 *(2.69)*	0.49 ± 0.12 *(3.09)*	0.50 ± 0.12 *(3.16)*	0.55 ± 0.14 *(3.55)*	0.53 ± 0.17 *(3.39)*	0.68 *(4.79)*
N	22	17	17	25	19	8	18	20	27	22	22	17	14	7	1
Mesopic positive contrast VA LE	0.28 ± 0.10 *(1.91)*	0.29 ± 0.09 *(1.95)*	0.33 ± 0.14 *(2.14)*	0.32 ± 0.13 *(2.09)*	0.30 ± 0.09 *(2.00)*	0.35 ± 0.10 *(2.24)*	0.35 ± 0.12 *(2.24)*	0.32 ± 0.10 *(2.09)*	0.41 ± 0.14 *(2.57)*	0.43 ± 0.13 *(2.69)*	0.50 ± 0.15 *(3.16)*	0.51 ± 0.09 *(3.24)*	0.52 ± 0.14 *(3.31)*	0.54 ± 0.13 *(3.47)*	0.66 *(4.57)*
N	21	17	16	24	19	7	19	20	27	21	22	17	14	7	1
Mesopic positive contrast VA Binocular	0.20 ± 0.09 *(1.58)*	0.17 ± 0.09 *(1.48)*	0.18 ± 0.09 *(1.51)*	0.19 ± 0.08 *(1.55)*	0.20 ± 0.11 *(1.58)*	0.22 ± 0.06 *(1.66)*	0.23 ± 0.10 *(1.70)*	0.21 ± 0.09 *(1.62)*	0.29 ± 0.12 *(1.95)*	0.33 ± 0.12 *(2.14)*	0.39 ± 0.12 *(2.45)*	0.38 ± 0.09 *(2.40)*	0.42 ± 0.17 *(2.63)*	0.44 ± 0.18 *(2.75)*	0.54 *(3.47)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Mesopic positive contrast VA Binocular	0.28 ± 0.13 *(1.91)*	0.27 ± 0.10 *(1.86)*	0.30 ± 0.12 *(2.00)*	0.31 ± 0.14 *(2.04)*	0.33 ± 0.10 *(2.14)*	0.35 ± 0.09 *(2.24)*	0.36 ± 0.13 *(2.29)*	0.31 ± 0.11 *(2.04)*	0.42 ± 0.15 *(2.63)*	0.44 ± 0.14 *(2.75)*	0.51 ± 0.13 *(3.24)*	0.50 ± 0.10 *(3.16)*	0.56 ± 0.15 *(3.63)*	0.57 ± 0.14 *(3.72)*	0.68 *(4.79)*

Table 5.9 Mean mesopic VA thresholds in logMAR, standard deviation and mean in minutes of arc per age bin of 5 years. Abbreviations: M = mean; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity; MOA = minutes of arc; RE = right eye; LE = left eye.

		b1	b2	b3	b4
Monocular Mesopic VA Negative Contrast	M	0.2441609772	0.093779238	30	0.0293961713
	UNL	0.5038813315	0.0893584033	30	0.0351806813
	LNL	-0.015215841	0.1263794482	30	0.0189793601
Monocular Mesopic VA Positive Contrast	M	0.3129855385	0.1259985774	30	0.0237526649
	UNL	0.5849517889	0.1311645385	30	0.0270318754
	LNL	0.0412487176	0.1348343644	30	0.0181197153
Binocular Mesopic VA Negative Contrast	M	0.1583942886	0.057827685	30	0.0367128897
	UNL	0.3738048409	0.0238437999	30	0.0640101483
	LNL	-0.050860053	0.08675	30	0.0189397399
Binocular Mesopic VA Positive Contrast	M	0.2024470363	0.0819290653	30	0.037837097
	UNL	0.4273609015	0.0830127636	30	0.0388676946
	LNL	-0.022125233	0.1199927094	30	0.0137950228

Table 5.10 Parameters of the Gauss-Newton formula for each mesopic VA measurement. Abbreviations: VA = visual acuity; M = mean; UNL = upper normal limit; LNL = lower normal limit.

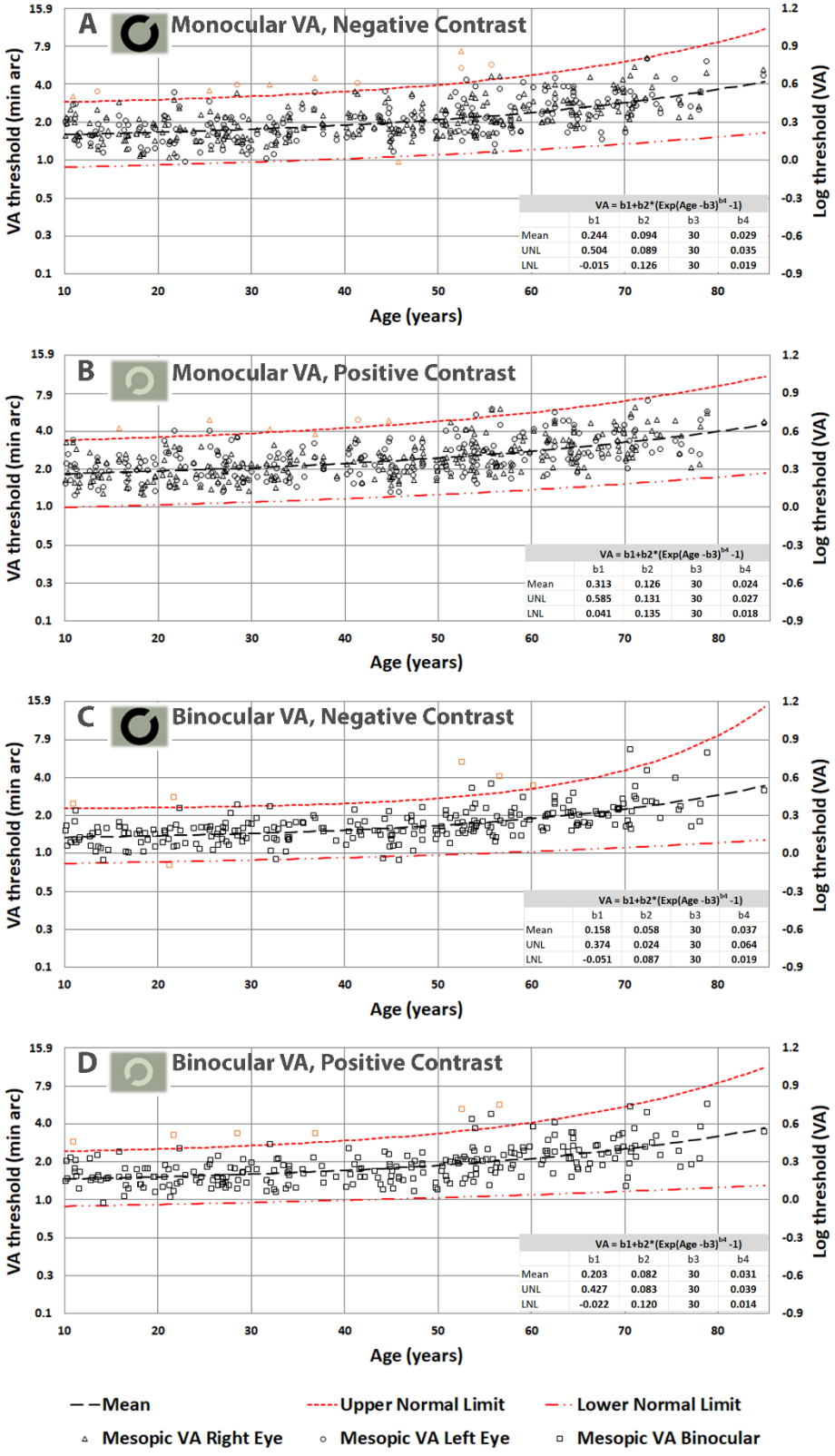


Figure 5.8 (A-D) Mesopic VA thresholds in logMAR units and the corresponding minutes of arc plotted as a function of age; monocular (right and left eye data) negative contrast (A), monocular (right and left eye data) positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D).

5.8 The effect of ageing on Photopic Functional Contrast Sensitivity

The mean FCS thresholds in percentages and standard deviations for each decade were calculated (table 5.11). Independent t-tests were performed to compare the thresholds for each decade with the subsequent decade. No differences were found up to the fifth decade. Significant differences (P<0.004) were found between the fifth and sixth decades for binocular negative contrast FCS and binocular positive contrast FCS. The difference between the sixth and seventh decade was statistically significant for positive contrast FCS for the right eye (P<0.004). The randomised monocular results revealed no significant differences between subsequent decades (P<0.004). The data points were divided in age bins of 5 years for monocular and binocular results of photopic negative and positive FCS similar to results for VA. The mean values in log and percentage for each 5 year age bin are shown in table 5.12. The non-linear Gauss-Newton function was fitted based on the mean and ±2.5σ of the age bins, to predict lower normal limits, means and upper normal limits of photopic FCS. Table 5.13 lists the parameters which describe means, upper and lower normal limits as a function of age.

	10-19 year	20-29 year	30-39 year	40-49 year	50-59 year	60-69 year	70-79 year	80-89 year
	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	log (%) *(PCT)*
N	38	41	26	39	49	38	21	1
Photopic negative contrast FCS RE	1.07 ± 0.16 *(11.75)*	1.08 ± 0.17 *(12.02)*	1.09 ± 0.17 *(12.30)*	1.12 ± 0.19 *(13.18)*	1.19 ± 0.21 *(15.49)*	1.35 ± 0.18 *(22.39)*	1.37 ± 0.25 *(23.44)*	1.89 *(77.62)*
N	38	42	27	38	48	39	21	1
Photopic negative contrast FCS LE	1.09 ± 0.14 *(12.30)*	1.05 ± 0.18 *(11.22)*	1.10 ± 0.16 *(12.59)*	1.12 ± 0.21 *(13.18)*	1.21 ± 0.18 *(16.22)*	1.33 ± 0.22 *(21.38)*	1.36 ± 0.21 *(22.91)*	1.60 *(39.81)*
N	39	42	26	39	49	38	21	1
Photopic negative contrast FCS Binocular	0.91 ± 0.15 *(8.13)*	0.90 ± 0.16 *(7.94)*	0.91 ± 0.13 *(8.13)*	0.94 ± 0.16 *(8.71)*	1.07 ± 0.18 *(11.75)*	1.18 ± 0.17 *(15.14)*	1.29 ± 0.23 *(19.50)*	1.55 *(35.48)*
N	39	42	27	39	50	39	21	1
Photopic negative contrast FCS Random	1.09 ± 0.16 *(12.30)*	1.09 ± 0.17 *(12.30)*	1.13 ± 0.19 *(13.49)*	1.12 ± 0.20 *(13.18)*	1.23 ± 0.21 *(16.98)*	1.35 ± 0.20 *(22.39)*	1.39 ± 0.25 *(24.55)*	1.89 *(77.62)*
N	39	41	26	38	49	39	21	1
Photopic positive contrast FCS RE	1.17 ± 0.17 *(14.79)*	1.15 ± 0.17 *(14.13)*	1.18 ± 0.16 *(15.14)*	1.15 ± 0.16 *(14.13)*	1.26 ± 0.19 *(18.20)*	1.40 ± 0.19 *(25.12)*	1.43 ± 0.27 *(26.92)*	1.92 *(83.18)*
N	38	42	27	38	49	38	21	1
Photopic positive contrast FCS LE	1.16 ± 0.15 *(14.45)*	1.15 ± 0.19 *(14.13)*	1.13 ± 0.18 *(13.49)*	1.18 ± 0.18 *(15.14)*	1.28 ± 0.19 *(19.05)*	1.37 ± 0.18 *(23.44)*	1.44 ± 0.18 *(27.54)*	1.77 *(58.88)*
N	39	42	26	38	49	39	21	1
Photopic positive contrast FCS Binocular	0.97 ± 0.15 *(9.33)*	0.97 ± 0.14 *(9.33)*	0.96 ± 0.13 *(9.12)*	0.99 ± 0.12 *(9.77)*	1.11 ± 0.20 *(12.88)*	1.24 ± 0.16 *(17.38)*	1.35 ± 0.24 *(22.39)*	1.49 *(30.90)*
N	39	42	27	39	50	39	21	1
Photopic positive contrast FCS Random	1.16 ± 0.17 *(14.45)*	1.15 ± 0.18 *(14.13)*	1.17 ± 0.20 *(14.79)*	1.18 ± 0.20 *(15.14)*	1.29 ± 0.22 *(19.50)*	1.41 ± 0.19 *(25.70)*	1.46 ± 0.25 *(28.84)*	1.92 *(83.18)*

Table 5.11 Mean photopic FCS thresholds in log (% contrast), standard deviation and mean in percentage per decade. Abbreviations: M = mean; log = logarithm; PCT = percentage; SD = standard deviation; FCS = functional contrast sensitivity; RE = right eye; LE = left eye.

	10-14 year	15-19 year	20-24 year	25-29 year	30-34 year	35-39 year	40-44 year	45-49 year	50-54 year	55-59 year	60-64 year	65-69 year	70-74 year	75-79 year	80-84 year
	M log (%) ± SD ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**log (%)** ***(PCT)***
N	21	17	17	24	18	8	19	20	27	22	21	17	14	7	1
Photopic negative contrast FCS RE	1.08 ± 0.16 *(12.02)*	1.06 ± 0.16 *(11.48)*	1.10 ± 0.18 *(12.59)*	1.07 ± 0.17 *(11.75)*	1.05 ± 0.12 *(11.22)*	1.17 ± 0.24 *(14.79)*	1.16 ± 0.20 *(14.45)*	1.08 ± 0.18 *(12.02)*	1.20 ± 0.18 *(15.85)*	1.19 ± 0.24 *(15.49)*	1.36 ± 0.18 *(22.91)*	1.35 ± 0.22 *(22.39)*	1.42 ± 0.32 *(26.30)*	1.42 ± 0.32 *(26.30)*	1.89 *(77.62)*
N	21	17	17	25	19	8	19	19	28	20	22	17	14	7	1
Photopic negative contrast FCS LE	1.11 ± 0.13 *(12.88)*	1.07 ± 0.15 *(11.75)*	1.05 ± 0.18 *(11.22)*	1.06 ± 0.19 *(11.48)*	1.08 ± 0.15 *(12.02)*	1.14 ± 0.18 *(13.80)*	1.19 ± 0.23 *(15.49)*	1.05 ± 0.18 *(11.22)*	1.23 ± 0.19 *(16.98)*	1.19 ± 0.16 *(15.49)*	1.32 ± 0.24 *(20.89)*	1.35 ± 0.18 *(22.39)*	1.34 ± 0.21 *(21.88)*	1.41 ± 0.21 *(25.70)*	1.60 *(39.81)*
N	22	17	17	25	18	8	19	20	28	21	21	17	14	7	1
Photopic negative contrast FCS Binocular	0.93 ± 0.15 *(8.51)*	0.88 ± 0.14 *(7.59)*	0.90 ± 0.15 *(7.94)*	0.91 ± 0.16 *(8.13)*	0.89 ± 0.12 *(7.76)*	0.97 ± 0.15 *(9.33)*	0.94 ± 0.17 *(8.71)*	0.95 ± 0.16 *(8.91)*	1.05 ± 0.19 *(11.22)*	1.09 ± 0.16 *(12.30)*	1.17 ± 0.17 *(14.79)*	1.19 ± 0.16 *(15.49)*	1.26 ± 0.20 *(18.20)*	1.34 ± 0.29 *(21.88)*	1.55 *(35.48)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Photopic negative contrast FCS Random	1.11 ± 0.16 *(12.88)*	1.05 ± 0.16 *(11.22)*	1.09 ± 0.18 *(12.30)*	1.08 ± 0.17 *(12.02)*	1.11 ± 0.19 *(12.88)*	1.16 ± 0.17 *(14.45)*	1.17 ± 0.22 *(14.79)*	1.08 ± 0.18 *(12.02)*	1.22 ± 0.19 *(16.60)*	1.24 ± 0.24 *(17.38)*	1.37 ± 0.21 *(23.44)*	1.33 ± 0.18 *(21.38)*	1.36 ± 0.24 *(22.91)*	1.45 ± 0.28 *(28.18)*	1.89 *(77.62)*

Table 5.12 (Continued)

	10-14 year	15-19 year	20-24 year	25-29 year	30-34 year	35-39 year	40-44 year	45-49 year	50-54 year	55-59 year	60-64 year	65-69 year	70-74 year	75-79 year	80-84 year
	M log (%) ± SD ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**log (%)** ***(PCT)***
N	22	17	17	24	18	8	18	20	27	22	22	17	14	7	1
Photopic positive contrast FCS RE	1.18 ± 0.16 *(15.14)*	1.17 ± 0.19 *(14.79)*	1.13 ± 0.19 *(13.49)*	1.17 ± 0.17 *(14.79)*	1.16 ± 0.14 *(14.45)*	1.21 ± 0.19 *(16.22)*	1.16 ± 0.13 *(14.45)*	1.13 ± 0.18 *(13.49)*	1.27 ± 0.18 *(18.62)*	1.25 ± 0.21 *(17.78)*	1.37 ± 0.17 *(23.44)*	1.45 ± 0.20 *(28.18)*	1.40 ± 0.22 *(25.12)*	1.48 ± 0.36 *(30.20)*	1.92 *(83.18)*
N	21	17	17	25	19	8	19	19	27	22	21	17	14	7	1
Photopic positive contrast FCS LE	1.18 ± 0.14 *(15.14)*	1.12 ± 0.16 *(13.18)*	1.14 ± 0.15 *(13.80)*	1.16 ± 0.22 *(14.45)*	1.11 ± 0.17 *(12.88)*	1.17 ± 0.21 *(14.79)*	1.24 ± 0.16 *(17.38)*	1.12 ± 0.18 *(18.18)*	1.27 ± 0.17 *(18.62)*	1.30 ± 0.21 *(19.95)*	1.37 ± 0.19 *(23.44)*	1.38 ± 0.16 *(23.99)*	1.43 ± 0.19 *(26.92)*	1.46 ± 0.18 *(28.84)*	1.77 *(58.88)*
N	22	17	17	25	18	8	19	19	28	21	22	17	14	7	1
Photopic positive contrast FCS Binocular	0.98 ± 0.17 *(9.55)*	0.96 ± 0.12 *(9.12)*	0.97 ± 0.14 *(9.33)*	0.97 ± 0.14 *(9.33)*	0.92 ± 0.12 *(8.32)*	1.04 ± 0.13 *(10.96)*	1.00 ± 0.11 *(10.00)*	0.97 ± 0.13 *(9.33)*	1.12 ± 0.22 *(13.18)*	1.11 ± 0.16 *(12.88)*	1.23 ± 0.18 *(16.98)*	1.25 ± 0.15 *(17.78)*	1.30 ± 0.21 *(19.95)*	1.43 ± 0.29 *(26.92)*	1.49 *(30.90)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Photopic positive contrast FCS Random	1.18 ± 0.16 *(15.14)*	1.14 ± 0.18 *(13.80)*	1.12 ± 0.18 *(13.18)*	1.18 ± 0.18 *(15.14)*	1.17 ± 0.22 *(14.79)*	1.16 ± 0.17 *(14.45)*	1.23 ± 0.20 *(16.98)*	1.14 ± 0.19 *(13.80)*	1.30 ± 0.22 *(19.95)*	1.28 ± 0.22 *(19.05)*	1.41 ± 0.19 *(25.70)*	1.41 ± 0.20 *(25.70)*	1.44 ± 0.25 *(27.54)*	*1.51* ± *0.26* *(32.36)*	1.92 *(83.18)*

Table 5.12 Mean photopic FCS thresholds in log (% contrast), standard deviation and mean in percentage per age bin of 5 years. Abbreviations: M = mean; log = logarithm; SD = standard deviation; PCT = percentage; FCS = functional contrast sensitivity; RE = right eye; LE = left eye.

		b1	b2	b3	b4
Monocular Photopic FCS Negative Contrast	M	1.1876846736	0.16598533	53	0.0389687207
	UNL	1.6512445754	0.2498369571	53	0.0378478176
	LNL	0.7183220855	0.0566666	53	0.0536215995
Monocular Photopic FCS Positive Contrast	M	1.238738738344	0.1283467571	51	0.0438171716
	UNL	1.6745292493	0.1332908794	51	0.0554206853
	LNL	0.7984492001	0.1231379082	51	0.0287500332
Binocular Photopic FCS Negative Contrast	M	1.0208345649	0.180821489	51	0.0395770268
	UNL	1.4220229963	0.1942186795	51	0.0483968556
	LNL	0.6157334061	0.1685074289	51	0.02776438
Binocular Photopic FCS Positive Contrast	M	1.0660654041	0.1473414401	51	0.0461074953
	UNL	1.4540220303	0.1861991756	51	0.0515320601
	LNL	0.67749366	0.1138304625	51	0.034037303

Table 5.13 Parameters of the Gauss-Newton formula for each photopic FCS measurement. Abbreviations: FCS = functional contrast sensitivity; M = mean; UNL = upper normal limit; LNL = lower normal limit.

Figure 5.9 (A-D) displays the photopic FCS thresholds for each study participant investigated. The descriptions of the best-fit model parameters of the means, upper and lower limits are presented in figure 5.9 (A-D). The mean photopic thresholds are constant and overall variability is minimal below 50 years of age. Above 50 years, both the mean thresholds and the observed inter-subject variability increase. In particular, the monocular results of both right eye and left eye data show more variability with increasing age. The positive contrast FCS thresholds appear to be more affected by age in comparison to the negative contrast FCS thresholds. The difference seems to be more pronounced in the monocular measurements compared to binocular measurements.

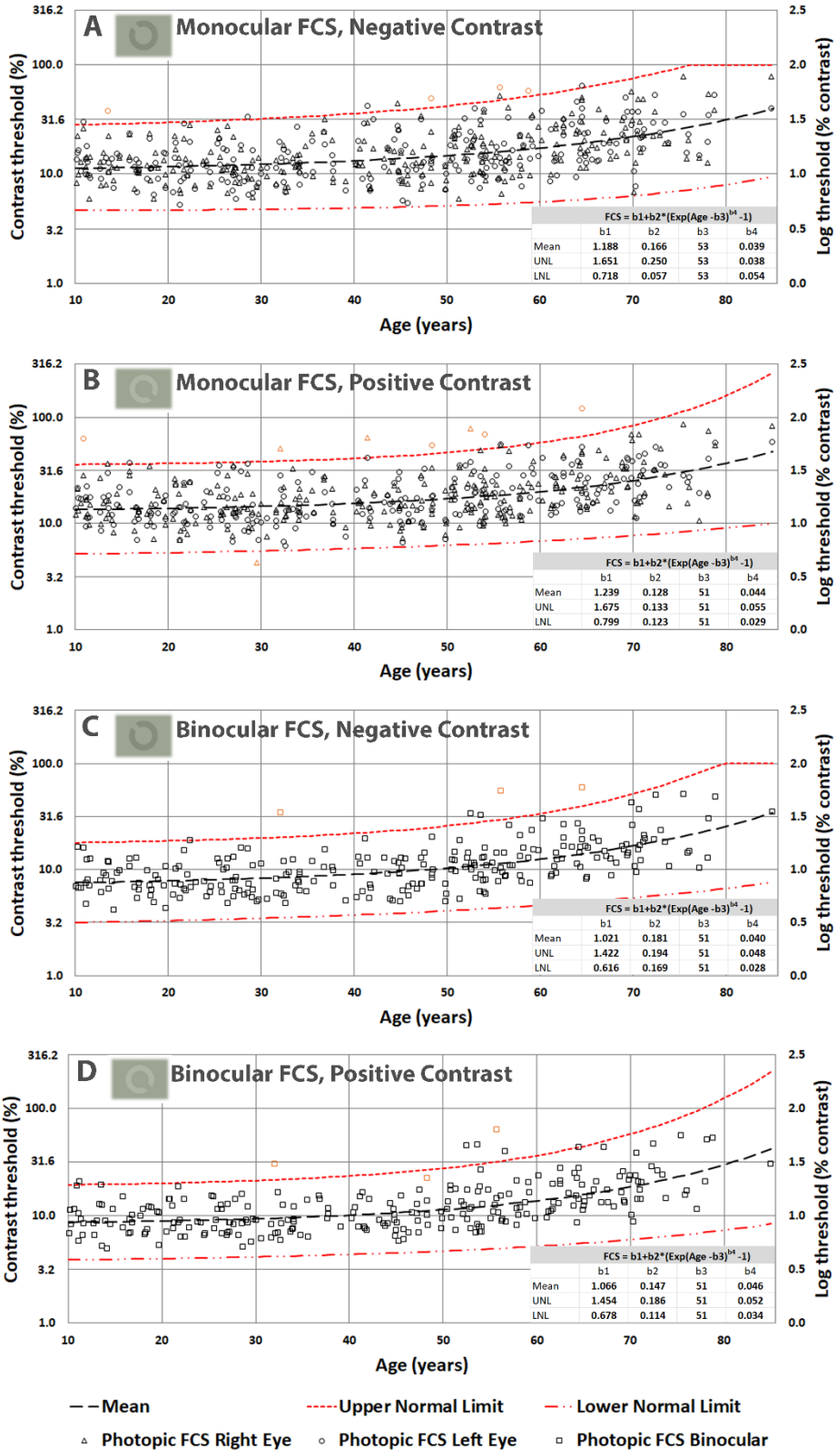


Figure 5.9 (A-D) Photopic FCS in log units and the corresponding percentage luminance contrast, plotted as a function of age; monocular (right and left eye data) negative contrast (A), monocular (right and left eye data) positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D).

5.9 The effect of ageing on Mesopic Functional Contrast Sensitivity

Mean mesopic FCS thresholds and standard deviations are shown in table 5.14 for each decade. To compare the thresholds of each decade with the subsequent decade, independent t-tests were performed. The differences were statistically significant (P<0.004) between the fifth and sixth decades for positive contrast FCS of the right eye, binocular negative contrast FCS and binocular positive contrast FCS. Between the sixth and seventh decades independent t-tests revealed statistically significant differences for negative contrast FCS of the right eye (P<0.004), negative contrast FCS of the left eye (P<0.004) and positive contrast FCS of the right eye (P<0.004). The randomised monocular results showed statistically significant differences for positive contrast FCS between the fifth and sixth decades (P<0.004) and in both contrast polarities between the sixth (P<0.004) and seventh decades (P<0.004).

The mean and ±2.5σ for mesopic FCS thresholds were calculated for bin sizes of 5 years. The mean values in percentage and log for each age bin are listed in table 5.15. The parameters of the proposed non-linear model were calculated using the Gauss-Newton method to obtain best-fit functions that predict the age dependence of mean values and lower and upper normal limits. The best-fit model parameters in table 5.16 describe each of the three fitted curves as a function of age. The monocular (all right eyes and left eyes) and binocular FCS thresholds measured with both negative and positive contrast using the mesopic protocol are displayed in figure 5.10 (A-D). In addition, this figure also plots the predictions of the model for the mean mesopic FCS thresholds as a function of age, together with the corresponding predictions for upper and lower normal threshold limits. The upper normal limits of FCS for mesopic monocular and binocular thresholds measured with negative contrast cannot exceed 2.00 log (100%). The results shown in figures 5.10 A and 5.10 C demonstrate clearly that some older, normal participants (above 45 years of age) are unable to resolve and locate the 3’ gap in a Landolt C optotype, even at the maximum contrast that can be produced. Compared with photopic conditions, mesopic FCS thresholds start increasing earlier with advancing age and show greater inter-participant variability.

	10-19 year	20-29 year	30-39 year	40-49 year	50-59 year	60-69 year	70-79 year	80-89 year
	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	M log (%) ± SD *(PCT)*	log (%) *(PCT)*
N	39	42	27	39	50	39	20	1
Mesopic negative contrast FCS RE	1.58 ± 0.19 *(38.02)*	1.59 ± 0.18 *(38.90)*	1.66 ± 0.16 *(45.71)*	1.68 ± 0.18 *(47.86)*	1.74 ± 0.16 *(54.95)*	1.86 ± 0.13 *(72.44)*	1.92 ± 0.09 *(83.18)*	2.00 *(100.00)*
N	39	42	27	39	49	39	20	1
Mesopic negative contrast FCS LE	1.56 ± 0.18 *(36.31)*	1.58 ± 0.20 *(38.02)*	1.60 ± 0.15 *(39.81)*	1.65 ± 0.17 *(44.67)*	1.76 ± 0.16 *(57.54)*	1.85 ± 0.13 *(70.79)*	1.90 ± 0.10 *(79.43)*	1.99 *(97.72)*
N	39	41	27	39	50	39	21	1
Mesopic negative contrast FCS Binocular	1.37 ± 0.17 *(23.44)*	1.40 ± 0.16 *(25.12)*	1.45 ± 0.15 *(28.18)*	1.45 ± 0.15 *(28.18)*	1.63 ± 0.19 *(42.66)*	1.73 ± 0.15 *(53.70)*	1.82 ± 0.15 *(66.07)*	1.95 *(89.13)*
N	39	42	27	39	50	39	21	1
Mesopic negative contrast FCS Random	1.57 ± 0.19 *(37.15)*	1.59 ± 0.19 *(38.90)*	1.63 ± 0.16 *(42.66)*	1.66 ± 0.17 *(45.71)*	1.75 ± 0.17 *(56.23)*	1.87 ± 0.11 (*74.13)*	1.91 ± 0.11 *(81.28)*	2.00 *(100.00)*
N	39	42	26	39	49	39	21	1
Mesopic positive contrast FCS RE	1.65 ± 0.19 *(44.67)*	1.68 ± 0.20 *(47.86)*	1.74 ± 0.15 *(54.95)*	1.74 ± 0.16 *(54.95)*	1.86 ± 0.15 *(72.44)*	1.98 ± 0.13 *(95.50)*	2.03 ± 0.18 *(107.15)*	2.25 *(177.83)*
N	39	42	27	38	50	39	21	1
Mesopic positive contrast FCS LE	1.64 ± 0.19 *(43.65)*	1.66 ± 0.21 *(45.71)*	1.70 ± 0.14 *(50.12)*	1.74 ± 0.15 *(54.95)*	1.85 ± 0.17 *(70.79)*	1.93 ± 0.14 *(85.11)*	1.97 ± 0.18 *(93.33)*	2.22 *(165.96)*
N	39	42	27	39	50	38	21	1
Mesopic positive contrast FCS Binocular	1.44 ± 0.16 *(27.54)*	1.48 ± 0.18 *(30.20)*	1.53 ± 0.16 *(33.88)*	1.55 ± 0.16 *(35.48)*	1.72 ± 0.21 *(52.48)*	1.80 ± 0.13 *(63.10)*	1.90 ± 0.22 *(79.43)*	2.11 *(128.82)*
N	39	42	27	39	50	39	21	1
Mesopic positive contrast FCS Random	1.63 ± 0.18 *(42.66)*	1.68 ± 0.20 *(47.86)*	1.71 ± 0.15 *(51.29)*	1.74 ± 0.15 *(54.95)*	1.86 ± 0.17 *(72.44)*	1.98 ± 0.14 *(95.50)*	2.03 ± 0.18 *(107.15)*	2.25 *(177.83)*

Table 5.14 Mean mesopic FCS thresholds in log (% contrast), standard deviation and mean in percentage per decade. Abbreviations: M = mean; log = logarithm; PCT = percentage; SD = standard deviation; FCS = functional contrast sensitivity; RE = right eye; LE = left eye.

	10-14 year	15-19 year	20-24 year	25-29 year	30-34 year	35-39 year	40-44 year	45-49 year	50-54 year	55-59 year	60-64 year	65-69 year	70-74 year	75-79 year	80-84 year
	M log (%) ± SD ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**log (%)** ***(PCT)***
N	22	17	17	25	19	8	18	20	28	22	22	17	13	7	1
Mesopic negative contrast FCS RE	1.58 ± 0.20 *(38.02)*	1.57 ± 0.19 *(37.15)*	1.60 ± 0.19 *(39.81)*	1.59 ± 0.17 *(38.90)*	1.64 ± 0.14 *(43.65)*	1.72 ± 0.21 *(52.48)*	1.71 ± 0.19 *(51.29)*	1.65 ± 0.16 *(44.67)*	1.76 ± 0.14 *(57.54)*	1.71 ± 0.18 *(51.29)*	1.86 ± 0.13 *(72.44)*	1.86 ± 0.13 *(72.44)*	*1.93* ± *0.09* *(85.11)*	1.90 ± 0.10 *(79.43)*	2.00 *(100.00)*
N	22	17	17	25	19	8	19	20	27	22	22	17	13	7	1
Mesopic negative contrast FCS LE	1.58 ± 0.19 *(38.02)*	1.53 ± 0.15 *(33.88)*	1.58 ± 0.21 *(38.02)*	*1.58* ± *0.21* *(38.02)*	1.56 ± 0.12 *(36.31)*	1.69 ± 0.17 *(48.98)*	1.70 ± 0.18 *(50.12)*	1.62 ± 0.16 *(41.69)*	1.75 ± 0.16 *(56.23)*	1.77 ± 0.16 *(58.88)*	1.84 ± 0.14 *(69.18)*	1.87 ± 0.11 *(74.13)*	1.87 ± 0.11 *(74.13)*	1.95 ± 0.05 *(89.13)*	1.99 *(97.72)*
N	22	17	16	25	19	8	19	20	28	22	22	17	14	7	1
Mesopic negative contrast FCS Binocular	1.36 ± 0.17 *(2.91)*	1.37 ± 0.16 *(23.44)*	1.41 ± 0.17 *(25.70)*	1.40 ± 0.15 *(25.12)*	1.42 ± 0.12 *(26.30)*	1.52 ± 0.19 *(33.11)*	1.49 ± 0.15 *(30.90)*	1.42 ± 0.14 *(26.30)*	1.59 ± 0.18 *(38.90)*	1.67 ± 0.20 *(46.77)*	1.72 ± 0.16 *(52.48)*	1.74 ± 0.14 *(54.95)*	1.80 ± 0.16 *(63.10)*	1.87 ± 0.13 *(74.13)*	1.95 *(89.13)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Mesopic negative contrast FCS Random	1.58 ± 0.20 *(38.02)*	1.55 ± 0.18 *(35.48)*	1.58 ± 0.18 *(38.02)*	1.60 ± 0.20 *(39.81)*	1.60 ± 0.15 *(39.81)*	1.69 ± 0.19 *(48.98)*	1.68 ± 0.19 *(47.86)*	1.64 ± 0.15 *(43.65)*	1.74 ± 0.17 *(54.95)*	1.76 ± 0.18 *(57.54)*	1.88 ± 0.12 *(75.86)*	1.86 ± 0.11 *(72.44)*	1.89 ± 0.12 *(77.62)*	1.94 ± 0.06 *(87.10)*	2.00 *(100.00)*

Table 5.15 (Continued)

	10-14 year	**15-19 year**	**20-24 year**	**25-29 year**	**30-34 year**	**35-39 year**	**40-44 year**	**45-49 year**	**50-54 year**	**55-59 year**	**60-64 year**	**65-69 year**	**70-74 year**	**75-79 year**	**80-84 year**
	M log (%) ± SD ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**M log (%) ± SD** ***(PCT)***	**log (%)** ***(PCT)***
N	22	17	17	25	19	7	18	20	28	21	22	17	14	7	1
Mesopic positive contrast FCS RE	1.67 ± 0.20 *(46.77)*	1.61 ± 0.17 *(40.74)*	1.67 ± 0.22 *(46.77)*	1.69 ± 0.20 *(48.98)*	1.71 ± 0.15 *(51.29)*	1.82 ± 0.11 *(66.07)*	1.76 ± 0.16 *(57.54)*	1.73 ± 0.16 *(53.70)*	1.88 ± 0.16 *(75.86)*	1.83 ± 0.14 *(67.61)*	1.97 ± 0.13 *(93.33)*	1.98 ± 0.13 *(95.50)*	2.04 ± 0.17 *(109.65)*	2.00 ± 0.21 *(100.00)*	2.25 *(177.83)*
N	22	17	17	25	19	8	18	20	28	22	22	17	14	7	1
Mesopic positive contrast FCS LE	1.66 ± 0.16 *(45.71)*	1.60 ± 0.14 *(39.81)*	1.65 ± 0.25 *(44.67)*	1.67 ± 0.19 *(46.77)*	1.66 ± 0.14 *(45.71)*	1.80 ± 0.09 *(63.10)*	1.76 ± 0.17 *(57.54)*	1.72 ± 0.14 *(52.48)*	1.83 ± 0.16 *(67.61)*	1.87 ± 0.19 *(74.13)*	1.94 ± 0.16 *(87.10)*	1.92 ± 0.12 *(83.18)*	1.94 ± 0.18 *(87.10)*	2.03 ± 0.14 *(107.15)*	2.22 *(165.96)*
N	22	17	17	25	19	8	19	20	28	22	21	17	14	7	1
Mesopic positive contrast FCS Binocular	1.49 ± 0.18 *(30.90)*	1.39 ± 0.12 *(24.55)*	1.48 ± 0.20 *(30.20)*	1.48 ± 0.16 *(30.20)*	1.50 ± 0.16 *(31.62)*	1.61 ± 0.15 *(40.74)*	1.56 ± 0.15 *(36.31)*	1.55 ± 0.18 *(35.48)*	1.71 ± 0.21 *(51.29)*	1.74 ± 0.21 *(54.95)*	1.80 ± 0.14 *(63.10)*	1.80 ± 0.10 *(63.10)*	1.90 ± 0.21 *(79.43)*	1.90 ± 0.21 *(79.43)*	2.11 *(128.82)*
N	22	17	17	25	19	8	19	20	28	22	22	17	14	7	1
Mesopic positive contrast FCS Random	1.67 ± 0.20 *(46.77)*	1.57 ± 0.14 *(37.15)*	1.65 ± 0.22 *(44.67)*	1.71 ± 0.19 *(51.29)*	1.67 ± 0.15 *(46.77)*	1.80 ± 0.11 *(63.10)*	1.74 ± 0.17 *(54.95)*	1.75 ± 0.14 *(56.23)*	1.85 ± 0.16 *(70.79)*	1.87 ± 0.19 *(74.13)*	1.99 ± 0.14 *(97.72)*	1.96 ± 0.14 *(91.20)*	2.03 ± 0.18 *(107.15)*	2.04 ± 0.21 *(190.65)*	2.25 *(177.83)*

Table 5.15 Mean mesopic FCS thresholds in log (% contrast), standard deviation and mean in percentage per age bin of 5 years. Abbreviations: M = mean; log = logarithm; SD = standard deviation; PCT = percentage; FCS = functional contrast sensitivity; RE = right eye; LE = left eye.

		b1	b2	b3	b4
Monocular Mesopic FCS Negative Contrast	M	1.6118294035	0.1875801785	30	0.0218072286
	UNL	2.0550261792	0.23561	30	0.0098546008
	LNL	1.1682515674	0.1788093303	30	0.0299749732
Monocular Mesopic FCS Positive Contrast	M	1.6947833147	0.2465537353	30	0.0189211516
	UNL	2.119276845	0.0550294922	30	0.0426579393
	LNL	1.2715693443	0.25362	30	0.020387954
Binocular Mesopic FCS Negative Contrast	M	1.4212097717	0.1956951592	30	0.0257030203
	UNL	1.8246968031	0.2620604243	30	0.0207193581
	LNL	1.0180292612	0.13690481	30	0.0325255124
Binocular Mesopic FCS Positive Contrast	M	1.5051476582	0.2643835506	30	0.0209095431
	UNL	1.9212189053	0.3104387298	30	0.0197618952
	LNL	1.0892196078	0.2236925744	30	0.0220624246

Table 5.16 Parameters for the Gauss-Newton formula for each mesopic FCS measurement. Abbreviations: FCS = functional contrast sensitivity; M = mean; UNL = upper normal limit; LNL = lower normal limit.

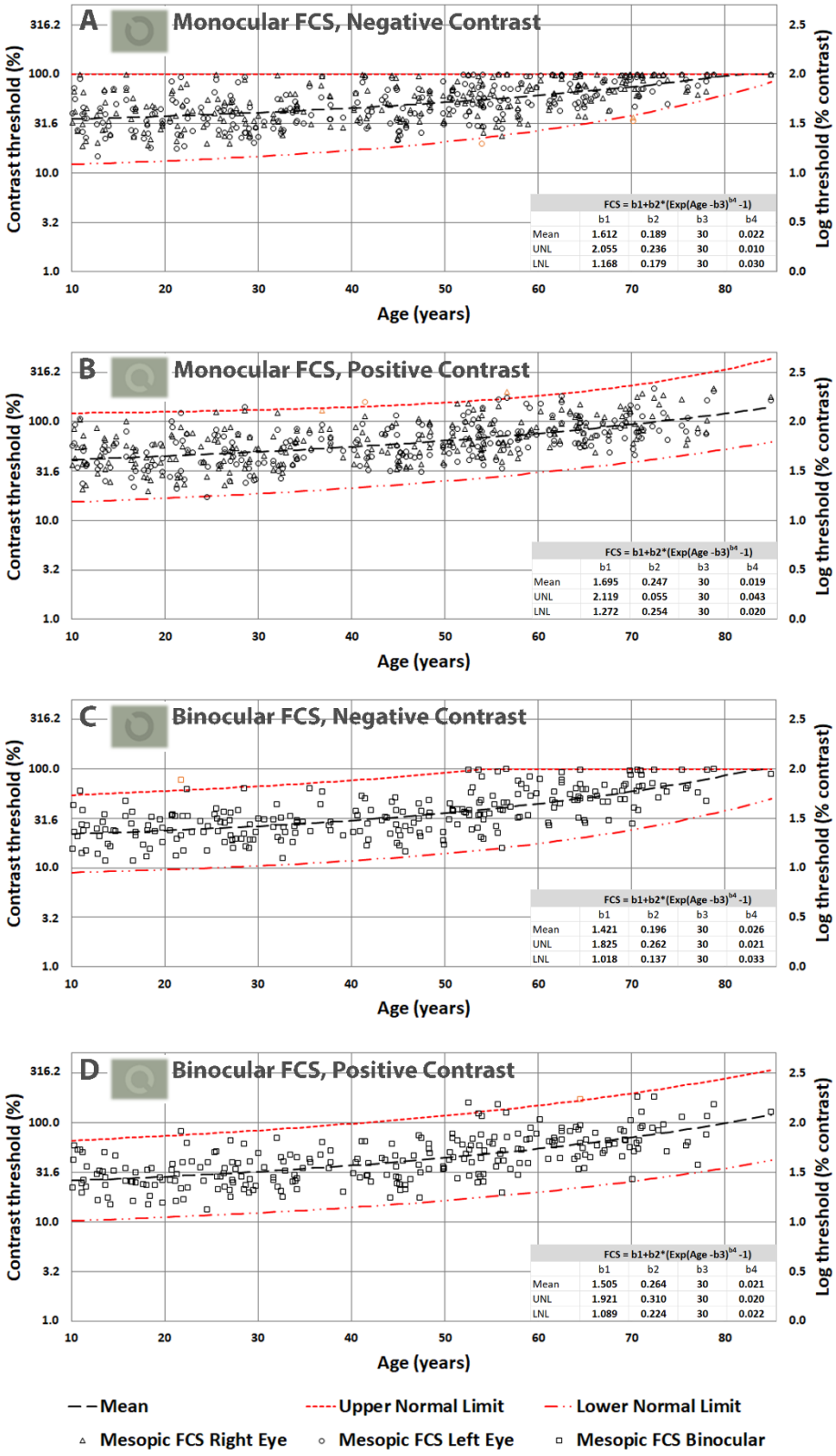


Figure 5.10 (A to D) Mesopic FCS in log units and the corresponding percentage luminance contrast, plotted as a function of age; monocular (right and left eye data) negative contrast (A), monocular (right and left eye data) positive contrast (B), binocular negative contrast (C) and binocular positive contrast (D). Since the maximum negative contrast of single optotypes cannot exceed 2.00 log units (100 %), some subjects cannot resolve the 3' gap size, even when presented at maximum contrast (see sections A and C). These results illustrate the large inter-

subject variability in contrast thresholds in the mesopic range. A few of the younger subjects have some difficulty with this task, even at 2.00 log units (100%) contrast (section A), but the majority of subjects above 60 years of age simply cannot do the task. Consequently, UNL thresholds of 2.00 log units (100%) plotted in sections A and C simply indicate that the subjects were unable to detect the gap at 2.00 log units (100%) contrast. As a result, the mean values will also be affected and the UNL are simply limited by the maximum negative contrast one can generate on the visual display.

6. Discussion

6.1 Discussion

The principal aim of this study was to establish how the 'healthy' normal ageing of the eye and visual pathways affect spatial vision under photopic and high mesopic lighting conditions. To achieve this aim, we needed a sensitive and efficient test of spatial vision to measure VA and FCS at photopic and high mesopic light levels. The Acuity-*Plus* test fulfils many of the requirements of this study. The test was designed to assess the effects of corneal refractive surgery on visual performance under photopic and mesopic lighting (Chisholm et al., 2003) and has more recently undergone improvements in stimulus parameters and methodology. Each standard protocol measures four parameters of interest which provide useful information on the participant's spatial vision. The interleaved measurement of these parameters minimizes the effects of other factors such as fatigue and variations in pupil size.
The Acuity-*Plus* test is a threshold contrast sensitivity test (Chisholm et al., 2003; Gillespie-Gallery et al., 2013). The differences between sinusoidal gratings tests and threshold contrast sensitivity tests have been a matter of debate for a long time. With sinusoidal gratings tests, the full CSF is established across a broad range of spatial frequencies. Threshold contrast sensitivity, such as letter contrast sensitivity, is the measurement of the smallest amount of luminance contrast required to detect, discriminate or identify a target. The contrast dependent mean luminance with letter contrast sensitivity is thought to introduce increased variability (Leguire, 1991). This can be rebutted by the systematic and identical increase of mean luminance in all charts (Pelli and Robson, 1991).
The use of different letters results in different orientations and spatial frequencies (Leguire, 1991). These differences are eliminated with the Acuity-*Plus* test by the use of the Landolt C. The crowding effect of letters is also described as a disadvantage in comparison to sinusoidal gratings (Leguire, 1991). However, the isolated Landolt C ring used in the Acuity-*Plus* test excludes the effect of crowding. Another problem described with some letter charts, for example the Regan chart, are the limited number of steps in contrast (Leguire, 1991). With computerised tests, such as the Acuity-*Plus* test, the number of contrast steps are unlimited. The sinusoidal gratings tests are based on detection, and the threshold contrast tests on identification. Very small optotypes result in larger differences between

discrimination and identification, and therefore between contrast threshold and sinusoidal gratings tests (Leguire, 1991).

The choice of optotype and optimum size have evolved over several years. Landolt rings with an outer diameter of 15 min of arc are frequently employed in such tests, largely because a gap size of 3 min of arc is considered functionally important in almost every occupation and at the same time is large enough to ensure that the majority of patients can carry out the task. A 15 min arc optotype is less affected by small residual refractive errors, large higher order aberrations and scattered light (Chisholm et al., 2003). A Landolt C optotype has additional advantages in that a four-alternative, forced response procedure can be implemented in a two-down, one-up staircase (Levitt, 1971), with variable step sizes which results in low chance probability (i.e., 1/16). This test procedure is statistically efficient and its implementation on calibrated visual displays which allows for the use of both luminance increments and decrements make this measurement of contrast thresholds appropriate for use in both occupations as well as in the clinic (Chisholm et al., 2003; Gillespie-Gallery et al., 2013). Furthermore, the contrast thresholds measured this way require the correct detection of the position of the gap in the Landolt ring and not the much lower contrast threshold needed to just detect the presence of the ring. As a result, the reciprocal of the contrast thresholds measured in this study yield much lower CS values. In order to distinguish the absolute measures of CS using sinusoidal gratings from functional tests that also measure contrast thresholds, but require either the naming of a letter or the correct localization of the gap in a Landolt ring, the reciprocal of the measured contrast threshold is described as FCS. In summary, the measurements of CS with sinusoidal gratings as a function of spatial frequency and visual field size yield a great deal of useful information, but take a long time to carry out and the results depend on the mode of stimulus presentation (e.g., briefly presented or drifting gratings) and the subject's threshold criterion (e.g., just noticeable bright or dark bars, motion direction, local flicker or just anything different to a uniform field) (Kelly, 1977; Rijsdijk, Kroon and van der Wildt, 1980). These disadvantages, particularly the long testing times, make full CS tests unattractive for use in the clinic. Patients are also more familiar with the test procedure of threshold contrast sensitivity (Regan, 1988). A compromise is to use constant size optotypes of varying luminance contrast and to measure the smallest contrast needed to just name the letters correctly (Pelli and Bex, 2013). Considering all the reasons described above, in this study the Acuity-*Plus* test was used. It is well known that some diseases affect threshold contrast sensitivity and sinusoidal gratings in a different manner

(Pelli and Robson, 1991). Therefore it is of importance to be aware that the results of different methods and tests are not interchangeable.

Our aim was the recruitment of a random sample of participants ranging from 10 to 90 years of age and to examine each participant according to predefined, healthy ageing criteria to ensure the exclusion of participants with loss of spatial vision that could be attributed to other factors. This task was particularly challenging for participants above 70 years of age. In the last two decades the aimed number of participants were not reached and/or the exclusion was significantly higher in comparison with the lower decades. The lower number of participants in the last two decades can be considered as limitation. The inter-subject variability increased significantly with advancing age and the lower number of participants beyond 70 years resulted in mean thresholds which are more susceptible to chance. Therefore, the results showed small improvement between mean thresholds of the older age groups for some measurements. In this study more females participated in comparison to males. Previous studies revealed differences in visual performance between males and females (Vanston and Strother, 2017). However, additional research is needed on sex differences at all levels of the visual system (Vanston and Strother, 2017). In this study, the differences between males and females were analysed for all photopic and mesopic measurements. No statistically significant differences were found for any of the measurements. By testing each eye separately, we were able to identify 27 participants as outliers as defined by statistically significant differences between the two eyes. The requirement to fulfil the exclusion criteria illustrated in figure 5.1 ensured that the participants selected for the study exhibited only gradual changes to the optics of the eye and the visual pathways that are commonly found in the normal population and can be attributed to the innumerable, gradual changes that affect the visual system in normal ageing.

An equation with four meaningful parameters was fitted to each set of data to allow prediction of VA and FCS for any age for each of the stimulus conditions investigated. The log transformed data measured for the majority of the tests carried out were found to be normally distributed and this allowed to use mean values and parametric tests for within and inter-subject comparisons. Some results, particularly those measured in older subjects using the mesopic conditions produced more residual skewness. Since these older participants passed the filtering conditions designed to screen for normal healthy vision, residual skewness of the data observed above 70 years of age is taken to reflect normal ageing. This and the observed increase in inter-subject variability with increasing age required the use of a non-linear model.

The model equation, $b_1 + b_2 * \{Exp (Age – b_3)^{b4} -1\}$, predicts well both the expected mean values as a function of age as well as the upper threshold limits needed to describe the effects of healthy normal ageing on spatial vision.

The model defined by the equation was fitted to each set of data points to predict mean values and ± 2.5σ limits. These functions describe normal gaining according to the selection criteria employed in the study. The b1 parameter reflects mean threshold values expected in young subjects before the effects of age become significant. Higher values for the b3 parameters, which vary around 50, in figures 5.7 (A-D) and 5.9 (A-D) and around 30, in figures 5.8 (A-D) and 5.10 (A-D) are indicative of the age above which the measured thresholds start to increase more rapidly. The higher rate of exponential increase becomes noticeable above 60 years of age and continues with increasing age, although extrapolation above 80 years of age is less justified because of fewer data points and potentially larger inter-subject variability. The largest thresholds and variability were measured with optotypes of positive contrast and correspond to the monocular viewing condition. The best performance for both VA and FCS is achieved in binocular viewing with negative contrast optotypes. The majority of participants exhibit large binocular summation.

In the mesopic condition, both VA and FCS start with much larger values (e.g., parameter b1 in the fitted model) and the measured thresholds start to increase more rapidly above 30 years of age. The inter-subject variability is also significantly larger in the mesopic range when compared to that measured for the corresponding age in the photopic range. VA and FCS thresholds, particularly in the photopic range appear to be stable with increasing age up to 50 years of age. Independent t-tests reveal significant differences (P<0.004) between mean thresholds per decade and the mean thresholds for the subsequent decade only above 50 years of age. These results are in general consistent with findings from other studies (Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Elliott, Yang and Whitaker, 1995; Sjöstrand et al., 2011).

In the high mesopic protocol, VA is reduced further and the decline in spatial vision begins earlier and becomes evident above 40 years of age. The results show that the increased variability also increases with age. The choice of 2 cd/m^2 for use in the Acuity-*Plus* protocol is consistent with typical residential street lighting and other mesopic working environments where adequate spatial vision is required (Wood, 2020; Li et al., 2020). Light levels below 0.2 cd/m^2 are considered to be more representative of the mesopic range, (Barbur and Stockman, 2010) but less representative of working environments which rarely fall below 2 cd/m^2 and also less useful clinically because of the much increased within and inter-subject variabilities.

The measurements of CS reveal similar findings and are largely consistent with the mesopic and photopic VA results. The decline in mesopic FCS is again more pronounced and the worsening of vision becomes more obvious above 50 years of age. These data are in general consistent with findings from previous studies (Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Gillespie-Gallery et al., 2013; Frisén and Frisén, 1981; Puell et al., 2004b). The results show that even in the high mesopic range, both VA and FCS are more susceptible to ageing than the corresponding findings in the photopic range.

It has been suggested that a number of different factors such as pupil miosis, increased scattered light and larger residual refractive errors can contribute to the reduction in VA and FCS with advancing age (Curcio et al., 1993; Haegerstrom-Portnoy, Schneck and Brabyn, 1999; Elliott, 1987). In addition, the slight decrease in cone photoreceptor density and the gradual loss of ganglion cells may also contribute to the worsening of spatial vision (Harwerth, Wheat and Rangaswamy, 2008; Panda-Jonas, Jonas and Jakobczyk-Zmija, 1995; Puell, Palomo-Álvarez and Pérez-Carrasco, 2018; Owsley, 2011). The flooring effect of the negative contrast FCS results, in particular under mesopic conditions, may be a limitation of this study. However, these FCS results showed the large inter-subject variability in the mesopic range. The maximum negative contrast of single optotypes cannot exceed 2.00 log (100%), and some of the participants were not been able to resolve the 3’ gap presented with the maximum contrast. The majority of these participants were above 60 years of age. The effective spatial contrast of a briefly presented stimulus is affected strongly by the temporal response function of the eye (Werner and Steele, 1988; Shinomori and Werner, 2003), and therefore it would be of interest to investigate the effect of presentation duration in these participants in future research. The normal limits for VA and FCS derived in this study can be used to identify subjects with parameters that fall outside normal age limits. It is not uncommon for an eye with increased higher order aberrations and scattered light to produce VA values outside normal range and FCS measured with larger stimuli well within the normal range. This is simply because the larger stimuli employed in FCS tests are less affected by higher order aberrations and forward light scatter in the eye. The best FCS one can achieve with larger stimuli is often limited by retinal sensitivity to contrast. Normal VA involves the use of much smaller stimuli which are more affected by both aberrations and scattered light (Elliott and Situ, 1998; Guirao et al., 1999). The opposite case also occurs when normal VA is accompanied by higher FCS. Such an outcome is consistent with good retinal image quality, but poor retinal sensitivity to contrast. Both VA and FCS are affected by the quality of the

retinal image, the level of retinal illuminance and the normal functioning of the retina. It is well established that retinal illuminance level affects strongly retinal sensitivity to contrast (Patterson, Bargary and Barbur, 2015), and that pupil miosis and changes in lens absorption with increasing age (van de Kraats and van Norren, 2007) cause progressive reduction in retinal illuminance in addition to reduction in retinal image contrast caused by increased forward scatter in the eye (Barbur and Stockman, 2010).

Cataract is the most common cause of decreased photopic and mesopic visual function for the reasons mentioned above (Chua, Mitchell and Cumming, 2004; Weiss, 1990; Elliott and Situ, 1998; Shandiz et al., 2011). In this study only participants with cataract gradings lower than or equal to two were included in the normal group on the basis that such changes are found commonly in older participants and hence can be taken to be representative of normal ageing.

In addition to the negative contrast tests that are normally used in clinical practice, VA and FCS in positive contrast have also been investigated in this study. The results measured with negative contrast optotypes were significantly better than the corresponding thresholds measured with positive contrast, in agreement with findings from earlier studies (Hwang and Peli, 2016). However, some studies found better performance with positive contrast optotypes (González et al., 2007; Westheimer et al., 2003). Another study with comparisons in two participants did not find differences in contrast thresholds when measured with negative and positive contrast stimuli (Alexander, Xie and Derlacki, 1993). Our findings suggest that threshold differences linked to the contrast polarity of the visual stimuli depend on age and light adaptation with the most pronounced differences found at lower light levels in older participants. In contrast, measurements with the FrACT test (Bach, 2007; Bach, 1996), which also employs Landolt ring stimuli, found no significant differences in photopic and scotopic VA between negative and positive contrast in young observers (Freundlieb et al., 2020). This may be due to the smaller sample size and also to the specific stimulus conditions of the study. The availability of open source software is attractive and it may make it possible to adjust the parameters of the test to approximate those employed in our study. Should this be the case, the use of fixed parameters that are similar to those employed in the Acuity-*Plus* test may well yield similar limits to those reported here. If so, the use of the spatial limits obtained in this study that describe the effects of aging under standardized conditions could be extended to other tests. The normal age-limits reported here are described fully and equations provided for each of the 16 stimulus viewing conditions. This makes it possible to compare our limits to those obtained with other

instruments, in addition to the FrACT test. The validation studies may not, however, be without challenges since the Acuity-*Plus* test employs a fully calibrated 10bit display and spectrally calibrated ND glasses for use in the mesopic protocol. Although this approach is of value in order to achieve standardized conditions, we acknowledge that in terms of general use, the more expensive calibrated equipment and the much higher dynamic range may limit the availability of the test. Although not included in this study, similar measurements carried out in participants with diabetes and other ocular conditions reveal much larger differences in both VA and FCS when comparing results measured with equivalent optotypes of opposite luminance contrast. Despite correlations between negative and positive VA and FCS contrast results being moderately strong, there was a lack of complete correlation, i.e. one might expect the correlation to be stronger given how closely these two functions are thought to be related. This observation suggests although both contrasts are reduced in a similar way by the optics of the eye, positive and negative contrast also reflect the involvement of independent stages of visual processing. These findings emphasized the importance of establishing age-related normal limits for both contrast polarities.

In the current study, both monocular and binocular VA and FCS were measured. Significant improvements in binocular thresholds are not unexpected given earlier findings (Pardhan, 1997; Gilchrist and Pardhan, 1987 ; Gillespie-Gallery et al., 2013). In this study, the advantage of binocular vision relative to monocular vision was also established for all measurements in photopic and mesopic conditions. It would be of interest to analyse the effect of binocular summation. However, given that this is not within the scope of this work we have not presented the findings in this thesis. It is well established that binocular summation decreases with age and some people experience inhibition (Gagnon and Kline, 2003; Pardhan, 1996). The decrease in binocular summation is often caused by an increase in interocular differences of VA and/or FCS with age (Pardhan, 1997; Haegerstrom-Portnoy, Schneck and Brabyn, 1999). The predicted binocular summation values are often smaller than what is practically observed. This finding suggests that neural interactions between the two eyes, neural summation, contribute to binocular summation (Campbell and Green, 1965).

The mean and upper normal age limits for VA and FCS measured both monocularly and binocularly with both positive and negative contrast optotypes make it possible to screen efficiently for normal spatial vision without any need for study-specific, normative data. This can be of significant advantage in many research studies, and is also of benefit in many visually demanding, occupational environments where

normal spatial vision is required at both photopic and high mesopic light levels. The inclusion of positive and negative contrast polarity and VA and FCS in the same test makes the results useful clinically for early detection of changes in the optics of the eye which affect the quality of the retinal image and also the presence of diseases of the retina that affect spatial vision. However, to use the established threshold limits of this study identical testing conditions of the Acuity-*Plus* need to be created in clinical settings or occupational settings.

A limitation of this study was the risk of unknown systemic disease. The decision on exclusion was based on history taking, and not a complete clinical health examination, including blood tests.

It has been reported that impaired mesopic acuity in clinically healthy eyes can precede AMD (Owsley et al., 2016a). It is also known that mesopic vision can be reduced in AMD risk genotype carriers, although the eyes are clinically normal. (Feigl et al., 2011). For that reason, the different filters were applied carefully and are likely to have excluded most of the participants with suspicious thresholds. However, in particular, follow-up data of the excluded participants based on interocular differences and outliers should be of interest. It could be possible that these suspicious thresholds precede any systemic and/or ocular disease.

The combination of the four measurements into one single test has significant advantages. In previous studies, VA and FCS were assessed using different test charts and also in different experimental sessions (Bühren et al., 2006; Yu et al., 2021). As a result, no standardized methods for measuring spatial vision using similar stimuli for both photopic and mesopic conditions have been produced. The choice of different parameters in different tests, such as the size of optotypes and the luminance and size of the adapting visual field make the comparison of results difficult and limit the usefulness of such measurements. In this study we placed great emphasis on justifying the choice of parameters for photopic and high mesopic conditions with direct reference to vision requirements within both occupations and also in the clinic.

Another important parameter in the Acuity-*Plus* test is the stimulus presentation time of ~ 160ms. This short time eliminates multiple fixations and minimizes within participant variability. In general the use of a short presentation time results in higher VA thresholds when compared to the same measurements under continuous viewing on ETDRS test chart (Heinrich, Kruger and Bach, 2010). In this study, the FCS thresholds measured with briefly presented stimuli were not compared directly against thresholds measured with longer stimuli or continuous viewing. Although this may be seen as a limitation in this study, the VA values measured in the photopic

protocol with brief stimuli in normal participants were similar to VA estimates measured on the same participants using ETDRS test chart in continuous viewing. The small improvement in VA thresholds measured on the ETDRS test chart may well be due to the much larger luminance of the ETDRS chart (~160 cd/m²) when compared to the background luminance employed in the Acuity-*Plus* test (32 cd/m²). The processing of clear edges and contours during brief presentations of the test stimulus requires normal temporal responses. Although the majority of participants with normal vision remain unaffected by the short stimulus presentation time with VA better than 1' (Snellen 6/6, see figure 5.7 C), older participants tend to be affected more, particularly at lower light levels. The brief presentation time may therefore make the test more sensitive when screening for early-stage ocular diseases, for example age-related macular degeneration. Such patients require much longer times to achieve best acuity compared to age-matched, healthy individuals (Kono and Yamade, 1996). Longer presentation times also result in multiple fixations and this can aid in the self-selection of the least-affected retinal area that yields the highest sensitivity. Recent studies have, however, shown that the temporal impulse response of the eye broadens and is less able to reproduce sharp temporal edges in older subjects (Shinomori and Werner, 2003; Werner and Steele, 1988). Significant loss of temporal responses have also been reported in patients with diabetes, glaucoma or age-related macular degeneration (Kono and Yamade, 1996). Since the effective spatial contrast of a briefly presented stimulus is affected strongly by the temporal response function of the eye, it is not surprising that when the latter is reduced either as a result of normal aging or disease, a high contrast, briefly presented stimulus is often equivalent to a continuously presented stimulus of lower contrast. Although the Acuity-*Plus* test measures VA and FCS, the measured parameters are also sensitive to changes in the temporal response characteristics of the retina.

Another limitation of this study may be the selection of the study population in three different settings. Two of the three testing sites were clinical settings; an optometry private practice and a university outpatient clinic. This may have resulted in a higher number of refractive errors, for example myopia, in comparison with a Dutch non-clinical population (Hendricks et al., 2009). However, visual functions in myopia are mainly affected in the higher range (>-6.00) (Liou and Chiu, 2001). In this study only a few participants were included with a higher degree of myopia. The prevalence of refractive errors are often based on habitual corrections. In this study each participant underwent a refraction and was corrected during the test. Even the participants with small ametropia without any complaints were classified as having a

refractive error. Furthermore, strict filters were applied to ensure that participants with suspicious thresholds were excluded. The selection of participants at three different settings can also be considered as strength when establishing normal age-related limits for occupational use. This choice ensured exposure to a variety of occupations and work-related visual tasks. Differences in test performance between the different sites were prevented by using the standard protocol of the test. The light conditions between the three locations were similar, and the same examiner carried out the examinations. Furthermore, all participants were Caucasian, and hence the use of the limits derived from this study with other ethnicities rests on the assumption that ethnicity-related differences in spatial vision are small.

Uncorrected refractive errors and astigmatism have been shown to affect VA and FCS (Hasegawa et al., 2018; Black et al., 2019; Woods, Strang and Atchison, 2000; Wolffsohn, Bhogal and Shah, 2011). In this study, each participant was refracted and corrected for the testing distance of 3m. Residual, uncorrected refractive errors are therefore unlikely to have affected significantly the measured thresholds.

In this study Bonferroni corrections were applied to adjust p values because of the risk of type 1 errors (rejecting a null hypothesis that is actually true in multiple testing) when conducting multiple statistical tests. To maintain the σ level over all tests at 0.05, the Bonferroni correction was applied to the p values for each individual test. However, the use of Bonferroni is controversial with one school of thought stating that correction must be applied in all multiple tests, and another stating that correction should never be made. If multiple tests are performed, there is an increase in the likelihood that one of the tests will be statistically significant by chance. However, there are also some arguments to conduct the analyses without Bonferroni correction. It could be argued that the evidence of a single statistical test should not be altered based on the number of other performed tests (Armstrong, 2014). Furthermore, by decreasing the risk of a type 1 error, the risk of a type 2 error (probability of accepting the null hypothesis when the alternative is true) increases (Armstrong, 2014). The adjusted p value decreases markedly when the number of tests increases, which result in lowering the power of the test (Armstrong, 2014). These arguments might suggest that the use of a correction is a limitation of this study. However, the conclusions of the majority of tests would have been similar when the conventional σ level of 0.05 was used.

In previous studies, different approaches were used when data was obtained from both eyes (Armstrong, 2013; Karakosta et al., 2012; Murdoch, Morris and Cousens, 1998; Fan, Teo and Saw, 2011). Data collected from both eyes are not independent and will be correlated, which need to be considered in the statistical analysis. In this

study comparisons were performed with the right and left eye results as independent data points, as well as by randomly selecting the right or left eye from each participant. The analyses with the randomly selected right or left eye from each participant are preferred if both eyes are eligible (Armstrong, 2013). In this study the conclusions of the comparisons are based on the tests performed with the randomised data. Again for completeness, comparisons within the individual eyes (right and left separately) are included in this thesis; the conclusions did not differ from those of the randomised data. To gain insight into the differences, results of both approaches are shown in the tables. The Pearson correlations were performed with the randomly selected right or left eye to obtain only independent observations.
The results of this study are of particular benefit for clinical and occupational use. Currently, visual function testing is often limited to photopic high contrast acuity, simply because measures of contract sensitivity are too demanding and require the investigation of several parameters using sinusoidal gratings, making the test often too long, complex and impractical in clinical practice (Pelli and Bex, 2013). However, the Acuity-*Plus* test is simple to carry out and, the availability of upper normal age limits for each of the four measured parameters may make this assessment valuable as part of the standard optometric examination. With the interleaved VA and FCS measurements, one examination for both tests is sufficient. Therefore, if clinicians had access to the test they would be able to establish contrast threshold earlier, which is more sensitive in the early detection and screening of ocular disease, in addition to high contrast acuity.
The measure of FCS introduced and investigated in this study relies on the measurement of only one luminance contrast for a fixed stimulus size. Since visually demanding tasks rarely employ alphanumeric characters smaller than three times the average acuity limit (i.e., 3x5'), the Landolt ring employed in the FCS test has an outer diameter of 15' with a 3' gap size. The ability to resolve and locate a 3' gap size in low contrast is functionally important in many visual tasks. The combined assessment of VA and FCS using photopic and high mesopic light levels with optotypes of positive and negative contrast provides a better description of the participant’s spatial vision.
Mesopic vision is strongly dependent of the luminance level within the mesopic range (Stockman and Sharpe, 2006; Barbur and Stockman, 2010). For this reason, it is of relevance that the mesopic VA and FCS were measured in precisely the same light conditions. Therefore within-participant comparison is possible between the different measurements. It will also contribute to consistency and reduced variability in repeated measurements. Combining the four parameters and the

availability of normal age limits can help in the early detection of retinal disease and may justify the use of the test in clinical practice. In particular, the mesopic measurements may be of interest in the early detection of retinal disease (Owsley et al., 2016a). With normal age-related VA and FCS limits well established, further investigations are needed to examine how these parameters can be used in the early detection of retinal disease. The standardized measurements can also be used to monitor the progression of ocular disease and to clarify patients' complaints in daily life activities under different lighting conditions. In addition, the normal VA and FCS age limits are also useful for use in clinical trials by eliminating the need for age-matched controls. The upper normal limits of spatial vision obtained in this study are also important in occupational environments when minimum spatial vision required are necessary to carry out visually demanding spatial tasks. This also applies equally to high mesopic lighting conditions which are typical of many working environments.

6.2 Conclusions

In photopic conditions VA, FCS and the overall variability were found to be age-invariant up to ~50 years. A lower, age-invariant limit of ~ 30 years was more appropriate for the mesopic range with a gradual, but accelerating increase in both mean thresholds and inter-subject variability above this age. Binocular thresholds were smaller and much less variable when compared with monocular results. Negative contrast optotypes results were significantly better than the corresponding results measured with positive contrast. This study has established upper normal, age limits for monocular and binocular viewing under photopic and high mesopic lighting with both positive and negative contrast optotypes using a single test which can be implemented in a clinic and occupational setting.

6.3 Recommendations future work

The participants in this study were examined by a full medical history and a thorough eye examination. However, not a complete health examination, including blood tests, was performed. With a novel developed method, filters were applied carefully and are likely to have excluded most of the participants with suspicious thresholds. However, in future studies, it would be of interest to exclude the risk of an unknown disease which can affect the eye by a full medical examination, including blood tests. This is idealistic, and a compromise could be to include a medical examination and blood tests of the most common diseases that can affect

the eye, such as diabetes. However, the filters applied to exclude the risks of unknown diseases remain important with a compromised method. It has been investigated that mesopic vision in clinically healthy eyes can be reduced in AMD risk genotypes (Feigl et al., 2011), and impaired mesopic vision can precede AMD development within three years (Owsley et al., 2016a). Therefore, a follow up of the excluded participants based on interocular difference and outliers should be of interest. The suspicious VA and/or FCS thresholds may precede any ocular or systemic disease which affect the eye. In this study, only Caucasian participants were included. Despite the fact that VA and FCS may not be affected by descent, it is of interest to investigate if the established age-related normal limits can be applied to other populations. Binocular summation has been documented in spatial vision, and seems to decline with age (Pardhan, 1996; Cagenello, Arditi and Halpern, 1993; Gillespie-Gallery et al., 2013; Gagnon and Kline, 2003). The decrease in binocular summation with age can be explained by age-related cortical cell loss and a decrease in photoreceptor activity (Gillespie-Gallery et al., 2013; Pardhan, 1996). In the current study, mean VA and FCS thresholds improved for all measurements binocularly in both light conditions. In a new study, the effect of binocular summation will be established. To determine the difference in binocular summation between the different light conditions and contrast polarities for both VA and FCS thresholds would be of interest. The established standardized protocol for both VA and FCS will result in comparable results between the different measurements and conditions.

7. Effect of systemic and ocular disease on spatial vision

7.1 Visual Acuity and common systemic disease

It is well established that systemic disease can involve the eye. Examples of disorders which can affect the eye are congenital (neurofibromatosis), traumatic, vascular (systemic hypertension, embolic disease, central retinal vein occlusion, migraine, hyperviscosity syndromes, sickle cell anemia), neoplastic (metastatic carcinoma), autoimmune (ankylosing spondylitis, systemic lupus erythematosus, polyarteritis or periarteritis nodosa, sarcoidosis, giant cell arteritis, thyroid disease, myasthenia gravis), idiopathic (multiple sclerosis), infectious (acquired immunodeficiency syndrome), metabolic/endocrine (diabetes) and drugs/toxins (Farber, 1988; Hazin, Lum and Daoud, 2012; Generali, Cantarini and Selmi, 2015; Rothenhaus and Polis, 1995). How VA is affected by systemic diseases depends on different factors, for example duration, severity and macular involvement.

7.1.1 Photopic Visual Acuity and common systemic diseases

Systemic disease may result in loss of VA. In diabetes for example, progression of the disease can lead to visual impairment (de Fine Olivarius et al., 2011). This is more likely in patients with advanced stages of diabetic retinopathy. However, some studies also found a decrease in VA in patients with diabetes without diabetic retinopathy (Brown et al., 2002). Measurements of low contrast VA seem to be more sensitive in patients with diabetes with ocular involvement compared with high contrast VA (Sukha and Rubin, 2009). Other diseases can affect VA performance indirectly, for example dry eye in patients with hyperthyroidism and rheumatoid arthritis (Fujita et al., 2005; Kashkouli et al., 2018; Abd-Allah et al., 2020). The effect of dry eye on spatial vision is well established (Szczotka-Flynn et al., 2019). In addition, the use of medication in systemic disease treatment can result in reduced VA. However, this is beyond the scope of the study and will not be discussed as part of this thesis.

7.1.2 Mesopic Visual Acuity and common systemic diseases

Little is known about mesopic VA in systemic disease. Evidence suggests, that diabetic retinopathy affects mesopic VA. It has been shown that treatment of

diabetic retinopathy is more effective on photopic VA in comparison with mesopic VA (Karatsai et al., 2021). It is expected that mesopic VA is also affected in patients with diabetes without retinopathy. Dry eyes as a result of systemic diseases, such as hyperthyroidism and rheumatoid arthritis, presumably affect mesopic VA. The tear film has a great impact on the optics of the eye as it is the first refracting component of the eye. It has been documented that dry eyes can cause an increase in irregular astigmatism and higher-order aberrations (Koh, 2018; Denoyer, Rabut and Baudouin, 2012), which may affect mesopic VA.

7.2 Visual Acuity and common ocular diseases

Visual function is affected by a number of ocular diseases, both inherited and acquired. Examples include age-related macular degeneration (AMD), cataract, glaucoma and cornea dystrophies or degenerations. VA can be affected by different amounts depending on the location and the severity of the ocular disease. For example, subtle VA changes in central serous retinopathy and mild cataract, to severe visual impairment in advanced AMD. In ocular disease visual performance under mesopic conditions is often more affected than under photopic conditions (Sunness et al., 1997). The effect of the presentation stimulus on spatial vision thresholds is also more pronounced in patients with optic neuropathies and retinal disease such as AMD. With longer stimulus presentation times, the effect of poor temporal responses can be reduced. A reduction of either stimulus presentation, contrast, or both worsens VA (Adrian, 2003).

7.2.1 Photopic Visual Acuity and common ocular diseases

Photopic VA is a poor indicator of progression in ocular diseases. For example, in glaucoma, photopic VA remains unaffected until the more advanced stages of the disease (Asaoka, 2013). The central region of the retina has more surviving ganglion cells than in the periphery (Curcio and Allen, 1990) which is likely to explain these findings. Visual field examination is therefore more sensitive in the screening of glaucoma progression.

Similar findings are observed in AMD, the third cause of blindness globally and the main cause in developed countries (Wong et al., 2014). In the more advanced stages of AMD VA will decrease significantly. It is well known that AMD affects daily life tasks, even in the early stages of the disease (Scilley et al., 2002). The results of the Rasch-calibrated NEI VFQ-25 scales in more advanced AMD patients were strongly associated with photopic high contrast VA and CS (Roh et al., 2018).

Pondorfer et al. (2020) measured photopic VA with the ETDRS letter chart (Pondorfer et al., 2020). Statistically significant VA differences were found between the early AMD group and the age-matched control group and between the intermediate AMD group and the controls. However, photopic high contrast VA was not sensitive enough to differentiate between early and intermediate AMD. In contrast, another study found no statistically significant differences between patients with early AMD compared to age-matched healthy individuals with the Bailey-Lovie letter chart (Puell et al., 2012).

Cataracts also influence the results of VA testing, depending upon the severity. Shandiz et al. (2011) reported that photopic VA is strongly associated with the cataract LOCS III grading (Shandiz et al., 2011). Although photopic VA alone is inadequate in predicting visual performance in everyday life tasks, additional tests such as CS with glare may be useful (Shandiz et al., 2011) and this will be discussed later on in the thesis (see section 7.3. and 7.4.).

In amblyopia photopic VA is decreased without ocular pathology, and is not correctable with glasses or contact lenses (Williams, 2009). Amblyopia is caused by absence of complete or partial visual input in one, or less frequently, to both eyes. Different types of amblyopia are stimulus deprivation amblyopia, unilateral/anisometropic amblyopia, strabismic amblyopia or bilateral refractive amblyopia. Amblyopia is often classified by photopic VA performance. VA of 6/9 to 6/12 corresponds with mild amblyopia, 6/12 to 6/36 with moderate amblyopia and worse than 6/36 with severe amblyopia (Williams, 2009). In unilateral amblyopia, VA performance in the fellow eye is excellent (Williams, 2009). The main focus on amblyopia treatment is improving VA.

7.2.2 Mesopic Visual Acuity and common ocular diseases

Despite the fact that photopic VA is a routine examination in clinical practice, mesopic VA is a more sensitive biomarker of ocular disease (Pondorfer et al., 2020). Mesopic vision is affected by several ocular diseases, for example hereditary conditions such as retinitis pigmentosa (Petzold and Plant, 2006). However, acquired ocular diseases such as vitamin A deficiency and AMD also affects mesopic vision (Petzold and Plant, 2006; Puell et al., 2012).

Patients with early stage AMD often complain of worse vision under mesopic luminance (Puell et al., 2012). Additionally, it is known that reading in low light conditions and night driving are often affected in patients with AMD (Brown et al., 1986; Scilley et al., 2002). Patients with AMD even experience difficulties with these

tasks when the fellow eye has relatively good performance (Scilley et al., 2002). As discussed previously, it is well known that visual performance in photopic conditions is better compared with mesopic conditions. The difference between photopic and mesopic VA is significantly greater in patients with AMD compared to healthy control participants (Puell et al., 2012). Puell et al. (2012) found statistically significant differences in mesopic high contrast VA between early AMD patients and age-matched controls, but not under photopic conditions. VA was measured using the Bailey-Lovie chart under photopic (85 cd/m2) and mesopic (0.1-0.2 cd/m^2) conditions. In another study, low luminance VA was also more sensitive in comparison with photopic VA to differentiate between three different groups; early AMD, intermediate AMD and age-matched controls (Pondorfer et al., 2020). Low illuminance VA has also been more sensitive in monitoring visual function in geographic AMD than photopic high contrast VA (Sunness et al., 2008; Sunness et al., 1997) and a better predictor of photopic VA loss in the future (Sunness et al., 2008). These findings are in agreement with several histopathological studies (Curcio et al., 1993). These studies demonstrated more severe loss of rods compared with cones in all stages of macular degeneration. Feigl et al. (2011) demonstrated that mesopic critical fusion frequency which requires the combined activity of cones and rods was significantly worse in carriers of AMD risk genotypes when compared to persons without risk genotypes (Feigl et al., 2011). All the risk genotypes carriers had clinically healthy eyes. Mesopic vision could therefore be a potential biomarker of subclinical AMD. These findings are in agreement with a study where impaired mesopic VA in individuals with a healthy macula was found to be a risk factor in developing AMD three years later (Owsley et al., 2016a). These findings are of interest in the early detection of AMD and these individuals may have benefit from advice of eye professionals about environmental factors such as diet, not smoking, supplements, and physical activity. The prevention of AMD could reduce the blindness caused by AMD and the associated costs of blindness.

Puell et al. (2013) found a relation between macular pigment optical density (MPOD) and VA (Puell et al.,). Participants with and without early AMD showed an improved high and low contrast VA with the Bailey-Lovie charts when the MPOD levels were high.

In accordance with photopic VA, mesopic VA showed decreased thresholds in amblyopic eyes (Mtanda et al., 1986; Singh and Agrawal, 2013). Mesopic VA may be of value in evaluating response to amblyopia treatment.

7.3 Contrast Sensitivity and common systemic disease

The effect of systemic disease on CS has been investigated, most commonly in diseases with the risk of ocular involvement, for example diabetic retinopathy (Pramanik et al., 2020). It has been documented that CS thresholds can be decreased, without any sign of diabetic retinopathy (Pramanik et al., 2020). CS may therefore be of interest in the early detection of ocular involvement in systemic disease.

7.3.1 Photopic Contrast Sensitivity and common systemic disease

In more advanced stages of systemic disease such as diabetes or hypertension CS is significantly decreased. In malignant hypertension spatial vision can be decreased (Steinegger, Bergin and Guex-Crosier, 2015). Furthermore, even in the absence of hypertensive retinopathy slight decrease in foveal sensitivity may be present (Eisner and Samples, 2003). Patients suffering from diabetic maculopathy or pre-proliferative/proliferative retinopathy have significantly reduced CS compared to controls (Verrotti et al., 1998; Abrishami et al., 2007; Khosla, Talwar and Tewari, 1991). However, patients with diabetes, but without retinopathy exhibited reduced CS as well (Arend et al., 1997; Rashmi et al., 2016). CS measurement may be useful in screening patients with diabetes, even before retinopathy is present. Using the VCTS 6500 test, Liska & Dostálek (1999), found that CS was a better descriptor of visual performance in insulin dependent patients with diabetes without retinopathy in comparison to high contrast Snellen VA (Liska and Dostálek, 1999). Similarly, in a small study of 30 participants Dosso et al. (1996) found that patients with diabetes without retinopathy showed a significant loss of CS compared to age-matched controls (Dosso et al., 1996). Measurements were made at an illuminance level of 85 cd/m^2 at three spatial frequencies; 6, 15 and 27 CPD.

Dosso et al. (1996) suggest that a diabetic induced increase in lens optical density may not be the only factor affecting CS (Dosso et al., 1996). Changes in the retina and its neural connection may precede detectable diabetic retinopathy (Dosso et al., 1996). The reduction of CS in diabetes could be attributed to tissue hypoxia (Harris et al., 1996). Harris et al. (1996) found an improvement of CS in early diabetic retinopathy patients when 100% oxygen was breathed (Harris et al., 1996). Increased age, nephropathy, and high systolic blood pressure were positively correlated with a decline in CS in patients with diabetes (Dosso et al., 1996). A positive correlation was also found between CS and metabolic control (Verrotti et al., 1998). The effect of Type 2 diabetes on CS was comparable to patients with Type 1

diabetes (Krasny et al., 2007). Krasny et al.'s study (2007) demonstrated that the CSV-1000 contrast test detected early retinal changes in Type 1 diabetes with good VA (Krasny et al., 2007).

7.3.2 Mesopic Contrast Sensitivity and common systemic disease

In comparison to photopic CS, less is known about the effect of diabetes on mesopic CS. Katz et al. (2010) measured CS using Gabor targets (frequencies 3 to 12 CPD) and found impaired foveal mesopic CS in patients with diabetes without retinopathy (Katz et al., 2010). They found a significant difference in foveal mesopic CS at a spatial frequency of 3 between patients with diabetes and controls. A more significant loss of mesopic foveal CS was found in the patients with diabetes, even though photopic high contrast was normal and OCT imaging showed no abnormalities. CS at higher spatial frequencies were low in both groups, lacking statistically significant differences. The mesopic measurements were taken at an illuminance level of 0.9 cd/m^2. In addition, CS was established under photopic conditions (20 cd/m^2). No differences were found between patients with diabetes and the control group. The results in the mesopic condition were in agreement with another study with a decline of mesopic CS in patients with diabetes without retinopathy (Dosso et al., 1996). With mesopic CS measurements, taken at an illuminance level of 5 cd/m^2 at spatial frequencies of 6, 15 and 27 CPD, a significant loss in CS was found in patients with diabetes. However, the same study found a significant loss of CS under photopic conditions. The decrease in both light conditions could be explained by neuro retinal changes before the onset of detectable diabetic retinopathy (Dosso et al., 1996). These results show that CS may be sensitive to the early decreases in visual function prior to the onset of diabetic retinopathy.

7.4 Contrast Sensitivity and common ocular disease

Both, photopic and mesopic CS are more sensitive to the early detection of visual changes in ocular disease when compared to VA alone (Maynard, Zele and Feigl, 2016; Müller et al., 2019; Bittner and Ferraz, 2020; Wai et al., 2021; Pondorfer et al., 2020; Midena et al., 1997; Roh et al., 2018; Feigl et al., 2011; Kleiner et al., 1988).

7.4.1 Photopic Contrast Sensitivity and common ocular disease

The effect of glaucoma on CS has been studied in multiple studies (Ansari, Morgan and Snowden, 2002; Lahav et al., 2011; Bierings et al., 2019; Bierings, de Boer and

Jansonius, 2018; Hertenstein et al., 2016). Photopic CS in patients with glaucoma was found to be significantly lower than in age-matched healthy individuals (Hertenstein et al., 2016; Bierings et al., 2019; Bierings, de Boer and Jansonius, 2018; Lahav et al., 2011; Ansari, Morgan and Snowden, 2002). Even in the early stages of glaucoma CS was poorer compared to controls (Ansari, Morgan and Snowden, 2002). This is in line with a study that demonstrated differences in foveal CS between glaucomatous and non-glaucomatous eyes with computerized psychophysical tests (Lahav et al., 2011). Despite good high contrast VA, foveal CS was significantly lower in the glaucomatous eyes, and a spatial frequency of 6 CPD correlated significantly with the stage of glaucoma. These results suggest that central CS measurement may be of interest in glaucoma screening, particularly since VA is not affected until later stages of glaucoma by which time the patients may be significantly visually impaired (Lahav et al., 2011).

Several studies determined that patients with early-stage AMD experience difficulty in daily life activities (Scilley et al., 2002; Owsley et al., 2006). In particular, activities with a strong dependence on good CS (e.g. recognizing faces, reading, road visibility) are difficult to perform in early AMD (Scilley et al., 2002). It is established that CS deficits are a better predictor of daily life activities. In patients with maculopathies caused by retinal vein occlusion, retinal detachment with macular involvement, dry and wet AMD, CS was significantly reduced when compared to age-matched controls, despite good high contrast VA (Wai et al., 2021). In that study CS was measured with the Manifold Platform (Adaptive Sensory Technology, San Diego, California, USA) at six spatial frequencies from 1 to18 CPD, which were all reduced with maculopathy except at 18 CPD.

These findings agree with other studies where CS has been found a sensitive biomarker in AMD (Midena et al., 1997; Kleiner et al., 1988). Puell et al. (2012) also found statistically significantly better performance in controls compared with early AMD patients using the Bailey-Lovie low contrast chart (10%) (Puell et al., 2012).

Previous studies showed that cataracts significantly lower CS under photopic conditions (Shandiz et al., 2011; Stifter et al., 2006). Shandiz et al. (2011) measured CS at four spatial frequencies (3,6,12 and 18 CPD) using the CSV-1000 contrast test. CS was reduced in all cataract types and at all spatial frequencies, and associated with increasing cataract severity following LOCS III grading.

It has also been documented that CS is decreased in amblyopic eyes, in particular for higher spatial frequencies (Chatzistefanou et al., 2005; Levi and Harwerth, 1977; Volkers et al., 1987). Lower CS thresholds for the fellow eye are also documented (Chatzistefanou et al., 2005). In amblyopic eyes where VA after treatment recovered

to 6/6, CS remains lower in comparison with controls (Wang et al., 2017). These results suggest that improvement of CS should be part of amblyopia treatment, as an alternative to VA alone.

7.4.2 Mesopic Contrast Sensitivity and common ocular disease

Patients with early-stage glaucoma experience more difficulty with daily living tasks, such as driving and reading, in low illuminance levels, compared with healthy individuals (Enoch et al., 2020; Tam et al., 2018; Khadka et al., 2016; Lorenzana et al., 2009).

As described previously (see section 7.4.1), photopic CS is affected by glaucoma, even in the early stages of the disease. It is also known that mesopic CS is affected in glaucoma patients (Bierings et al., 2019; Bierings, de Boer and Jansonius, 2018; Lahav et al., 2011; Hertenstein et al., 2016). The differences between patients suffering from glaucoma and age-matched healthy individuals were more pronounced under mesopic conditions than photopic conditions (Bierings, de Boer and Jansonius, 2018; Lahav et al., 2011; Hertenstein et al., 2016). Bierings et al. (2018) also investigated the CS in photopic and mesopic conditions peripherally (Bierings, de Boer and Jansonius, 2018). Under both lighting conditions, differences between patients with glaucoma and age-matched controls were also statistically significant in the periphery, although they were more pronounced in mesopic conditions. Owsley et al. (2006) asked patients with AMD to self-reported difficulty in activities of daily living under low luminance conditions by using a newly developed questionnaire (Owsley et al., 2006). The questionnaire was divided into six subscales; driving, extreme lighting conditions, mobility, emotional distress, general dim lighting problems and peripheral vision. They found a statistically significant relationship between dark adaptation parameters and the scores on all subscales. Maynard et al. (2016) concluded that using the Pelli-Robson chart in AMD patients under mesopic conditions, changes in visual function were detected earlier compared to photopic measurements (Maynard, Zele and Feigl, 2016). This is in agreement with the finding that mesopic low contrast VA with the Bailey-Lovie low contrast chart (10%) is more affected by early AMD than under photopic conditions (Puell et al., 2012).

Amblyopic eyes with decreased VA showed a decreased performance with mesopic CS (Levi and Harwerth, 1977). Photopic VA is the most important determinant in the evaluation of amblyopia treatment. However, CS measurements in photopic and mesopic conditions should be considered in amblyopia management.

It is of interest to investigate how the established normal VA and FCS limits in both light conditions can be applied in the screening of systemic and ocular conditions. This is a highly exploratory study in patients with ocular and systemic conditions commonly seen in a general optometric practice. This study was not conducted to analyse the effect of the different conditions on photopic and mesopic VA and FCS.

7.5 Methods

The excluded participants with systemic and ocular conditions were not involved in determining age-related normal limits for spatial vision in different light conditions. These participants were divided into subgroups, such as systemic vascular conditions, systemic non-vascular conditions, fundus abnormalities, amblyopia and anterior segment conditions. The VA and FCS results of these groups were fitted in a graph against the normal lower and upper limits established in chapter 5. The effects of lens opacities on VA and FCS thresholds were assessed in the participants who remained after the selection filters for normal photopic and mesopic visual performance. To analyse the effect of lens opacities on VA and FCS thresholds, independent t-tests were conducted for each decade separately to exclude the effect of normal ageing. The independent t-tests were performed for the right and left eye results, and the Bonferroni correction was applied due to multiple comparisons.

7.6 Results

7.6 Effect of systemic disease on Photopic Visual Acuity and Functional Contrast Sensitivity

This section will apply the established upper normal limits of photopic VA in participants with systemic conditions. Due to a small number of participants within the different groups the results need to be considered as a pilot study. Photopic and mesopic results of systemic vascular and non-vascular disorders will be described consecutively.

7.6.1 Vascular conditions

As described in the previous sections, no statistically significant differences in VA and FCS were found between participants with hypertension and age-matched healthy individuals. The systemic vascular conditions group consisted of participants with the following conditions: diabetes (3), diabetes and hypertension (6), hyperlipidimia (7) and cardiovascular disease (4). None of the participants had any

signs of retinopathy. Table 7.1 describes the participants according to their systemic vascular condition and presents all photopic measurements of the participants. In addition, for each measurement, the upper normal limits were calculated for the specific age of the participant. Regarding the group with diabetes, one of the three participants had a borderline threshold, which means that the threshold falls on the boundary of the upper normal limit. These thresholds should be considered as clinically abnormal. For the left eye photopic FCS negative contrast was borderline. One of the six participants with diabetes and hypertension had a threshold outside the normal limit for positive contrast VA. One participant with hyperlipidemia had thresholds outside the upper normal limits or borderline for each measurement with at least one of both eyes. From the participants with cardiovascular disease, one showed a threshold outside the normal limit for photopic positive contrast VA and a borderline threshold for negative contrast VA of the left eye. Each individual's photopic VA and FCS measurement was plotted against the means, upper normal limits and lower normal limits of participants with normal visual performance established in this thesis (figure 7.1 (A-D)). In the graph, the participant identification numbers are placed next to their left eye measurement, corresponding to the participant in the table. The corresponding right eye results can be found along the same x-axis location in line with the left eye results.

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Diabetes								
26 RE	0.34 *(2.20)*	0.42 *(2.63)*	0.34 *(2.18)*	0.46 *(2.88)*	1.60 *(40.08)*	1.76 *(57.54)*	1.69 *(48.97)*	1.79 *(61.66)*
26 LE	0.38 *(2.42)*		0.31 *(2.04)*		**1.76 *(58.02)***		1.67 *(47.07)*	
68 RE	0.23 *(1.71)*	0.46 *(2.88)*	0.17 *(1.47)*	0.50 *(3.16)*	1.34 *(21.65)*	1.85 *(70.79)*	1.51 *(32.03)*	1.89 *(77.62)*
68 LE	0.08 *(1.19)*		0.16 *(1.45)*		1.30 *(20.11)*		1.32 *(20.95)*	
140 RE	-0.06 *(0.87)*	0.42 *(2.63)*	0.02 *(1.05)*	0.46 *(2.88)*	1.03 *(10.73)*	1.76 *(57.54)*	1.09 *(12.34)*	1.79 *(61.66)*
140 LE	0.09 *(1.22)*		0.19 *(1.56)*		0.96 *(9.16)*		1.25 *(17.62)*	
Diabetes and Hypertension								
20 RE	0.44 *(2.73)*	0.50 *(3.16)*	0.33 *(2.14)*	0.52 *(3.31)*	1.70 *(50.58)*	1.92 *(83.18)*	1.74 *(54.33)*	1.98 *(95.50)*
20 LE	0.18 *(1.50)*		0.13 *(1.36)*		1.50 *(31.72)*		1.50 *(31.97)*	
24 RE	0.23 *(1.68)*	0.40 *(2.51)*	0.23 *(1.71)*	0.44 *(2.75)*	1.42 *(26.28)*	1.71 *(51.29)*	1.46 *(28.57)*	1.75 *(56.23)*
24 LE	0.21 *(1.62)*		0.12 *(1.31)*		1.13 *(13.58)*		1.41 *(25.67)*	
28 RE	0.37 *(2.36)*	0.49 *(3.09)*	**0.59 *(3.87)***	0.51 *(3.24)*	1.77 *(58.86)*	1.90 *(79.43)*	1.90 *(79.31)*	1.95 *(89.13)*
28 LE	-0.02 *(0.96)*		0.13 *(1.36)*		1.42 *(26.08)*		1.47 *(29.61)*	
76 RE	0.12 *(1.31)*	0.44 *(2.75)*	0.05 *(1.12)*	0.48 *(3.02)*	1.37 *(23.23)*	1.81 *(64.57)*	1.32 *(20.68)*	1.84 *(69.18)*
76 LE	0.25 *(1.79)*		0.18 *(1.52)*		1.53 *(34.19)*		1.39 *(24.45)*	
323 RE	0.27 *(1.87)*	0.60 *(3.98)*	0.36 *(2.27)*	0.59 *(3.89)*	1.64 *(44.13)*	2.00 *(100.00)*	1.73 *(54.18)*	2.24 *(173.78)*
323 LE	0.58 *(3.79)*		0.54 *(3.45)*		1.99 *(97.13)*		2.03 *(108.33)*	
372 RE	0.41 *(2.55)*	0.53 *(3.39)*	0.37 *(2.32)*	0.55 *(3.55)*	1.75 *(56.63)*	1.99 *(97.72)*	1.80 *(63.62)*	2.06 *(114.82)*
372 LE	0.32 *(2.11)*		0.28 *(1.90)*		1.65 *(45.06)*		1.70 *(49.89)*	
Hyperlipidemia								
10 RE	0.08 *(1.21)*	0.43 *(2.69)*	0.16 *(1.46)*	0.46 *(2.88)*	1.29 *(19.56)*	1.77 *(58.88)*	1.21 *(16.04)*	1.81 *(64.57)*
10 LE	0.12 *(1.31)*		0.18 *(1.51)*		1.16 *(14.54)*		1.12 *(13.17)*	
105 RE	-0.01 *(0.98)*	0.36 *(2.29)*	0.15 *(1.42)*	0.40 *(2.51)*	1.12 *(13.04)*	1.63 *(42.66)*	1.12 *(13.25)*	1.68 *(47.86)*
105 LE	0.04 *(1.09)*		0.12 *(1.31)*		1.13 *(13.46)*		1.24 *(17.33)*	
190 RE	0.35 *(2.26)*	0.41 *(2.57)*	0.36 *(2.31)*	0.45 *(2.82)*	1.68 *(47.69)*	1.75 *(56.23)*	1.50 *(31.30)*	1.78 *(60.26)*
190 LE	0.24 *(1.77)*		0.32 *(2.05)*		1.70 *(49.82)*		1.56 *(36.38)*	
194 RE	0.10 *(1.27)*	0.49 *(3.09)*	0.03 *(1.06)*	0.52 *(3.31)*	1.26 *(18.10)*	1.90 *(79.43)*	1.22 *(16.63)*	1.96 *(91.20)*
194 LE	-0.03 *(0.93)*		0.10 *(1.27)*		1.15 *(14.13)*		19.43 *(1.29)*	
303 RE	0.15 *(1.42)*	0.42 *(2.63)*	0.20 *(1.59)*	0.46 *(2.88)*	1.28 *(18.95)*	1.77 *(58.88)*	1.35 *(22.33)*	1.80 *(63.10)*
303 LE	0.25 *(1.77)*		0.25 *(1.77)*		1.29 *(19.49)*		1.30 *(19.80)*	
320 RE	**0.49 *(3.10)***	0.44 *(2.75)*	0.46 *(2.91)*	0.47 *(2.95)*	**1.82 *(66.20)***	1.80 *(63.10)*	1.80 *(62.72)*	1.84 *(69.18)*
320 LE	**2.92 (0.66)**		**2.92 (0.47)**		**1.81 *(65.29)***		**1.92 *(82.94)***	

Table 7.1 (Continued)

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Hyperlipidemia								
370 RE	0.22 *(1.67)*	0.47 *(2.95)*	0.49 *(3.12)*	0.50 *(3.16)*	1.64 *(44.11)*	1.86 *(72.44)*	1.72 *(52.70)*	1.90 *(79.43)*
370 LE	0.18 *(1.52)*		0.20 *(1.59)*		1.21 *(16.17)*		1.28 *(19.24)*	
Cardiovascular Disease								
246 RE	0.11 *(1.28)*	0.42 *(2.63)*	0.26 *(1.84)*	0.46 *(2.88)*	1.41 *(25.82)*	1.76 *(57.54)*	1.49 *(31.24)*	1.80 *(63.10)*
246 LE	0.40 *(2.52)*		0.34 *(2.19)*		1.69 *(48.99)*		1.63 *(42.46)*	
368 RE	0.40 *(2.49)*	0.61 *(4.07)*	0.33 *(2.16)*	0.60 *(3.98)*	1.76 *(57.75)*	2.00 *(100.00)*	1.73 *(53.96)*	2.28 *(190.55)*
368 LE	**0.61** ***(4.04)***		**0.72** ***(5.28)***		1.97 *(94.20)*		2.20 *(153.93)*	
371 RE	0.15 *(1.42)*	0.45 *(2.82)*	0.06 *(1.16)*	0.48 *(3.02)*	1.27 *(18.64)*	1.82 *(66.07)*	1.25 *(17.59)*	1.86 *(72.44)*
371 LE	0.05 *(1.13)*		0.10 *(1.27)*		1.37 *(23.30)*		1.41 *(25.43)*	
376 RE	0.21 *(1.63)*	0.48 *(3.02)*	0.23 *(1.69)*	0.51 *(3.24)*	1.59 *(39.25)*	1.89 *(77.62)*	1.73 *(53.41)*	1.94 *(87.10)*
376 LE	0.15 *(1.41)*		0.17 *(1.47)*		1.41 *(25.58)*		1.55 *(35.27)*	

Table 7.1 Photopic VA thresholds in logMAR and photopic FCS thresholds in log (% contrast) of participants with systemic vascular disorders. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.1. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

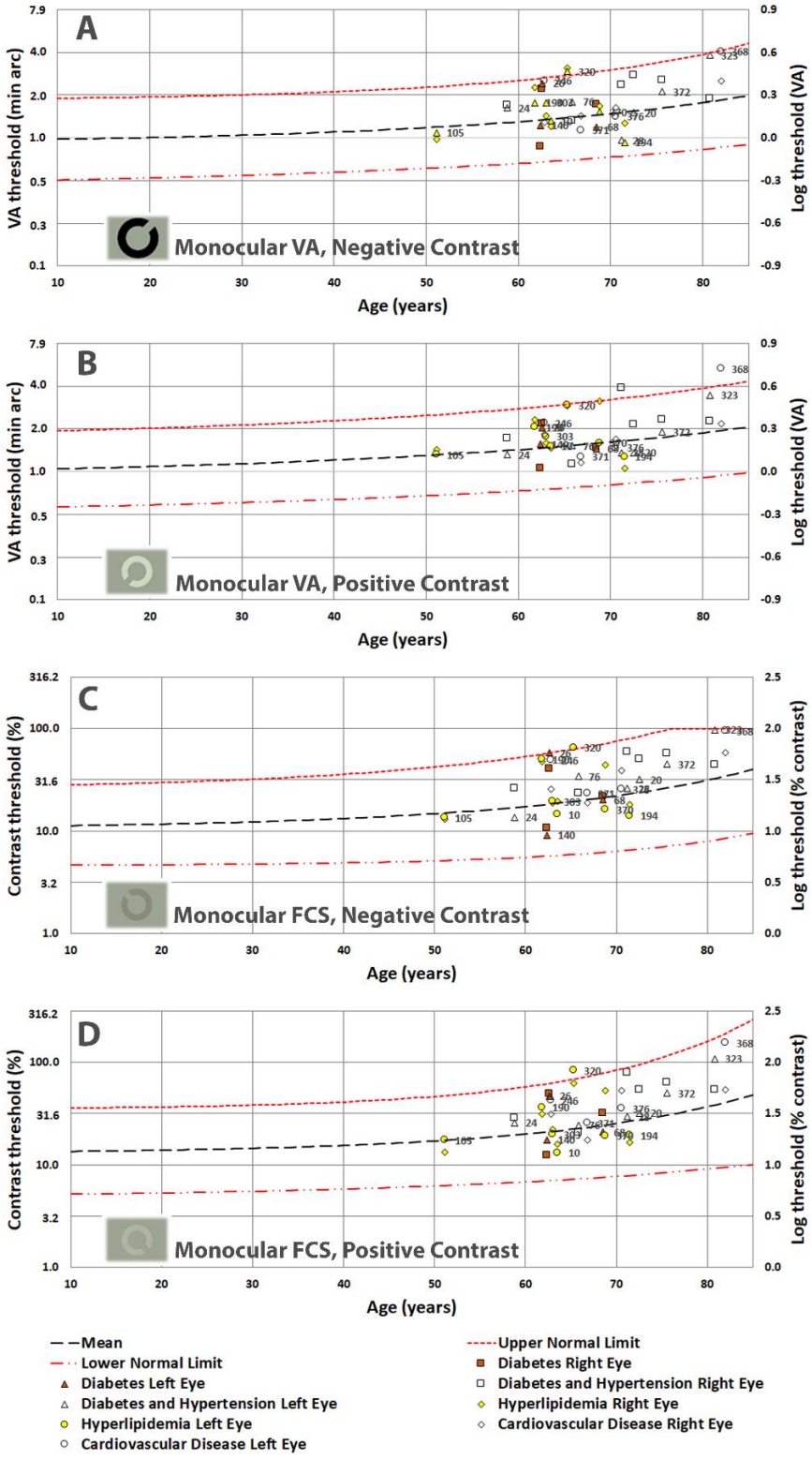


Figure 7.1 (A-D) Photopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with vascular systemic conditions plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of photopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.6.2 Non-vascular conditions

Participants in the non-vascular conditions group were divided into the following sub-groups: rheumatoid arthritis (4), allergic rhinitis (3), asthma (4) and other systemic conditions (11). The other systemic conditions group consisted of participants with conditions such as hypothyroidism, hyperthyroidism, epilepsy, multiple sclerosis, ulcerative colitis and attention deficit hyperactivity disorder (ADHD). The photopic negative and positive VA and FCS thresholds of the participants with rheumatoid arthritis, allergic rhinitis, asthma, hypothyroidism and hyperthyroidism were all within the upper normal limits. One participant with epilepsy had thresholds outside the upper normal limits for photopic negative contrast FCS and positive contrast FCS of the right eye. The negative contrast VA threshold was borderline. The participants with ulcerative colitis and multiple sclerosis had thresholds within the normal range for all measurements. Visual performance was established in two participants with ADHD. One of them had an abnormal threshold for photopic positive contrast VA of the right eye, the other revealed thresholds outside normal range in all photopic measurements with the exception of negative and positive contrast VA of the right eye. The results for the participants with non-vascular systemic conditions are listed in table 7.2 and illustrated in figure 7.2 (A-D).

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Rheumatoid Arthritis								
61 RE	0.14 *(1.39)*	0.34 *(2.14)*	0.27 *(1.86)*	0.38 *(2.40)*	1.42 *(26.45)*	1.59 *(38.90)*	1.39 *(24.61)*	1.64 *(43.65)*
61 LE	-0.01 *(0.98)*		0.12 *(1.33)*		1.35 *(22.28)*		1.19 *(15.43)*	
213 RE	0.05 *(1.12)*	0.31 *(2.04)*	0.00 *(1.01)*	0.34 *(2.19)*	1.15 *(14.00)*	1.52 *(33.11)*	1.16 *(14.60)*	1.59 *(38.90)*
213 LE	0.10 *(1.25)*		0.04 *(1.10)*		1.16 *(14.56)*		1.20 *(15.67)*	
237 RE	-0.04 *(0.91)*	0.32 *(2.09)*	*-0.08* *(0.83)*	0.36 *(2.29)*	0.77 *(5.83)*	1.55 *(35.48)*	0.91 *(8.21)*	1.61 *(40.74)*
237 LE	0.03 *(1.08)*		0.12 *(1.31)*		1.19 *(15.43)*		1.19 *(15.66)*	
259 RE	*0.00* *(0.99)*	0.33 *(2.14)*	-0.08 *(0.83)*	0.37 *(2.34)*	1.10 *(12.72)*	1.58 *(38.02)*	1.15 *(14.03)*	1.63 *(42.66)*
259 LE	0.03 *(1.07)*		0.08 *(1.19)*		1.04 *(10.88)*		1.20 *(15.95)*	
Allergic Rhinitis								
109 RE	-0.05 *(0.90)*	0.34 *(2.19)*	-0.02 *(0.96)*	0.38 *(2.40)*	1.14 *(13.83)*	1.60 *(39.81)*	1.14 *(13.65)*	1.64 *(43.65)*
109 LE	-0.14 *(0.73)*		0.07 *(1.17)*		1.08 *(11.96)*		1.10 *(12.51)*	
215 RE	-0.06 *(0.87)*	0.30 *(2.00)*	-0.06 *(0.88)*	0.33 *(2.14)*	1.18 *(15.15)*	1.51 *(32.36)*	1.11 *(12.96)*	1.58 *(38.02)*
215 LE	0.02 *(1.04)*		0.06 *(1.15)*		1.04 *(10.99)*		1.08 *(11.96)*	
255 RE	0.12 *(1.31)*	0.31 *(2.04)*	0.16 *(1.44)*	0.34 *(2.19)*	1.24 *(17.49)*	1.53 *(33.88)*	1.31 *(20.27)*	1.60 *(39.81)*
255 LE	0.23 *(1.71)*		0.31 *(2.06)*		1.50 *(31.65)*		1.51 *(32.07)*	
Asthma								
119 RE	0.03 *(1.08)*	0.44 *(2.75)*	0.02 *(1.05)*	0.48 *(3.02)*	1.26 *(18.40)*	1.80 *(63.10)*	1.21 *(16.17)*	1.84 *(69.18)*
119 LE	0.14 *(1.37)*		0.13 *(1.34)*		1.48 *(30.28)*		1.44 *(27.60)*	
154 RE	-0.16 *(0.69)*	0.28 *(1.91)*	0.14 *(1.38)*	0.29 *(1.95)*	1.08 *(11.98)*	1.45 *(28.18)*	1.35 *(22.34)*	1.56 *(36.31)*
154 LE	0.03 *(1.06)*		0.11 *(1.29)*		1.02 *(10.36)*		1.14 *(13.88)*	
185 RE	0.21 *(1.63)*	0.38 *(2.40)*	0.26 *(1.82)*	0.42 *(2.63)*	1.29 *(19.25)*	1.68 *(47.86)*	1.38 *(23.92)*	1.72 *(52.48)*
185 LE	0.25 *(1.77)*		0.39 *(2.46)*		1.24 *(17.29)*		1.61 *(40.36)*	
270 RE	-0.11 *(0.78)*	0.36 *(2.29)*	-0.02 *(0.96)*	0.40 *(2.51)*	0.99 *(9.81)*	1.64 *(43.65)*	1.19 *(15.45)*	1.68 *(47.86)*
270 LE	0.00 *(1.01)*		0.09 *(1.22)*		1.09 *(12.42)*		1.11 *(12.91)*	
Other Systemic Conditions Hypothyroidism								
62 RE	-0.07 *(0.86)*	0.31 *(2.04)*	-0.25 *(0.56)*	0.34 *(2.19)*	0.88 *(7.61)*	1.52 *(33.11)*	0.90 *(7.96)*	1.59 *(38.90)*
62 LE	0.05 *(1.12)*		0.06 *(1.16)*		1.04 *(11.06)*		1.23 *(16.81)*	
304 RE	-0.04 *(0.91)*	0.36 *(2.29)*	0.06 *(1.16)*	0.40 *(2.51)*	1.24 *(17.43)*	1.65 *(44.67)*	1.06 *(11.40)*	1.69 *(48.98)*
304 LE	0.23 *(1.69)*		0.24 *(1.74)*		1.29 *(19.55)*		1.31 *(20.26)*	
Hyperthyroidism								
153 RE	0.27 *(1.88)*	0.49 *(3.09)*	0.27 *(1.86)*	0.51 *(3.24)*	1.39 *(24.44)*	1.90 *(79.42)*	1.59 *(39.07)*	1.95 *(89.13)*
153 LE	0.26 *(1.84)*		0.24 *(1.73)*		1.56 *(36.07)*		1.40 *(25.31)*	
340 RE	0.22 *(1.65)*	0.42 *(2.63)*	0.27 *(1.86)*	0.46 *(2.88)*	1.43 *(26.75)*	1.76 *(57.54)*	1.37 *(23.64)*	1.79 *(61.66)*
340 LE	0.03 *(1.08)*		0.01 *(1.02)*		1.28 *(19.15)*		1.32 *(20.92)*	

Table 7.2 (Continued)

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Hyperthyroidism								
356 RE	0.28 *(1.91)*	0.60 *(3.98)*	0.34 *(2.20)*	0.60 *(3.98)*	1.48 *(30.28)*	2.00 *(100.00)*	1.46 *(28.62)*	2.24 *(173.78)*
356 LE	0.19 *(1.54)*		0.21 *(1.64)*		1.39 *(24.33)*		1.45 *(27.93)*	
Epilepsy								
77 RE	-0.04 *(0.92)*	0.34 *(2.19)*	0.01 *(1.03)*	0.38 *(2.40)*	1.13 *(13.42)*	1.59 *(38.90)*	1.11 *(13.01)*	1.64 *(43.65)*
77 LE	-0.05 *(0.90)*		-0.11 *(0.78)*		0.99 *(9.80)*		1.01 *(10.24)*	
296 RE	**0.34** ***(2.18)***	0.34 *(2.19)*	0.35 *(2.25)*	0.38 *(2.40)*	**1.76** ***(57.92)***	1.60 *(39.81)*	**1.65** ***(44.64)***	1.64 *(43.65)*
296 LE	0.21 *(1.61)*		0.20 *(1.58)*		1.38 *(24.21)*		1.42 *(26.54)*	
Multiple Sclerosis								
329 RE	-0.03 *(0.93)*	0.39 *(2.45)*	0.05 *(1.13)*	0.43 *(2.69)*	1.07 *(11.69)*	1.70 *(50.12)*	1.16 *(14.53)*	1.73 *(53.70)*
329 LE	0.14 *(1.30)*		0.15 *(1.41)*		1.08 *(12.14)*		1.10 *(12.67)*	
Ulcerative Colitis								
170 RE	-0.08 *(0.84)*	0.31 *(2.04)*	0.08 *(1.20)*	0.33 *(2.14)*	1.11 *(12.92)*	1.52 *(33.11)*	1.21 *(13.23)*	1.59 *(38.90)*
170 LE	-0.11 *(0.77)*		0.01 *(1.03)*		0.98 *(9.54)*		1.13 *(13.56)*	
Attention deficit hyperactivity disorder								
146 RE	0.15 *(1.40)*	0.28 *(1.91)*	0.22 *(1.65)*	0.29 *(1.95)*	**1.65** ***(44.45)***	1.46 *(28.84)*	**1.74** ***(54.64)***	1.56 *(36.31)*
146 LE	**0.29** ***(1.94)***		**0.37** ***(2.32)***		**1.82** ***(66.48)***		**1.82** ***(66.38)***	
252 RE	0.05 *(1.13)*	0.30 *(2.00)*	**0.35** ***(2.25)***	0.33 *(2.14)*	1.21 *(16.09)*	1.51 *(32.36)*	1.40 *(25.18)*	1.58 *(38.02)*
252 LE	-0.02 *(0.95)*		0.20 *(1.58)*		1.05 *(11.35)*		1.15 *(14.03)*	

Table 7.2 Photopic VA thresholds in logMAR and photopic FCS thresholds in log (% contrast) of participants with systemic non-vascular disorders. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.2. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

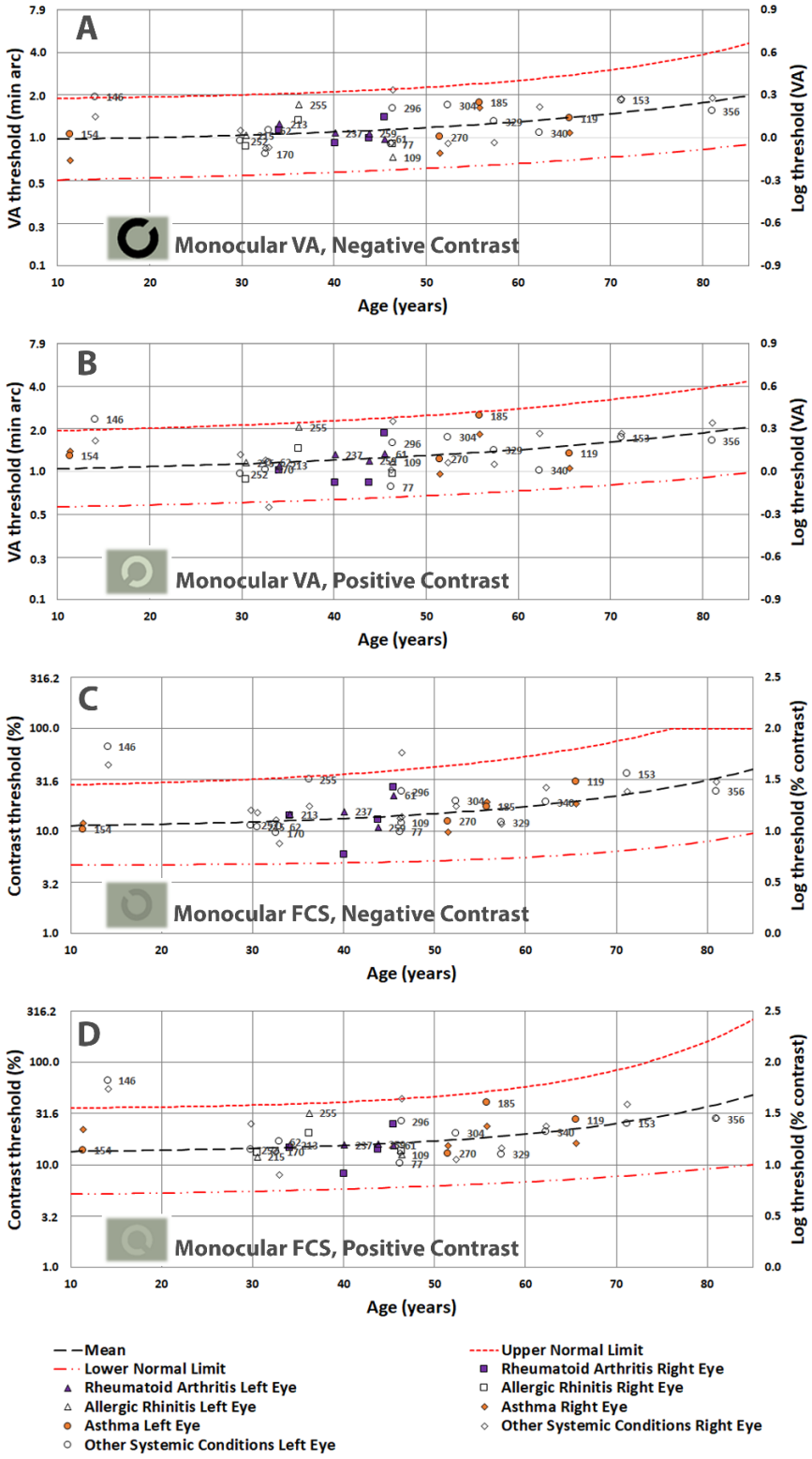


Figure 7.2 (A-D) Photopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with non-vascular systemic conditions plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of photopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.7 Effect of systemic disease on Mesopic Visual Acuity and Functional Contrast Sensitivity

In the following sections, mesopic VA and FCS thresholds of participants with systemic conditions will be compared to the upper normal limits of the corresponding age. The same participants with systemic diseases described in section 7.6 also participated in these measurements.

7.7.1 Vascular conditions

One of the three participants with diabetes showed abnormal mesopic VA thresholds. This participant had thresholds outside normal limits for both eyes with mesopic VA negative contrast, and with mesopic VA positive contrast and mesopic FCS positive contrast, for the right and left eye respectively. It should be noted that in more participants the mesopic FCS negative contrast thresholds were borderline or very close to the maximum of 2.00 log (100%). In the participants suffering from both diabetes and hypertension, one had a threshold outside normal limits for the right eye with mesopic positive contrast FCS. Four participants had borderline negative contrast FCS thresholds or very close to 2.00 log (100%) and should be considered clinically abnormal. Three of the seven participants with hyperlipidemia showed abnormal thresholds for one or more mesopic measurements. Out of the four individuals with cardiovascular disease, one had thresholds outside the normal limit for positive contrast VA and positive contrast FCS of the left eye. Two participants showed borderline thresholds of negative contrast FCS for at least one eye. Table 7.3 shows all the thresholds for each participant and these values are plotted in figure 7.3 (A-D) with the means, upper normal limits and lower normal limits established on normally sighted individuals.

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Diabetes								
26 RE	**0.79** ***(6.17)***	0.70 *(5.01)*	**0.84** ***(6.87)***	0.77 *(5.89)*	**2.00** ***(99.62)***	2.00 *(100.00)*	2.20 *(159.90)*	2.29 *(194.98)*
26 LE	**0.80** ***(6.36)***		0.69 *(4.89)*		1.99 *(98.12)*		**2.36** ***(230.74)***	
68 RE	0.44 *(2.73)*	0.76 *(5.75)*	0.58 *(3.80)*	0.83 *(6.76)*	1.98 *(95.91)*	2.00 *(100.00)*	2.20 *(157.68)*	2.35 *(223.87)*
68 LE	0.33 *(2.16)*		0.36 *(2.28)*		1.83 *(68.06)*		1.92 *(83.49)*	
140 RE	0.23 *(1.71)*	0.69 *(4.90)*	0.35 *(2.25)*	0.77 *(5.89)*	1.56 *(36.66)*	2.00 *(100.00)*	1.83 *(68.16)*	2.28 *(190.55)*
140 LE	0.21 *(1.63)*		0.36 *(2.30)*		1.56 *(35.95)*		1.85 *(71.00)*	
Diabetes and Hypertension								
20 RE	0.61 *(4.04)*	0.81 *(6.46)*	0.62 *(4.15)*	0.87 *(7.41)*	1.99 *(98.50)*	2.00 *(100.00)*	2.12 *(131.28)*	2.40 *(251.19)*
20 LE	0.52 *(3.32)*		0.50 *(3.18)*		1.86 *(72.67)*		1.99 *(98.74)*	
24 RE	0.51 *(3.25)*	0.66 *(4.57)*	0.51 *(3.24)*	0.74 *(5.50)*	1.91 *(80.67)*	2.00 *(100.00)*	1.94 *(87.35)*	2.25 *(177.83)*
24 LE	0.33 *(2.12)*		0.45 *(2.80)*		1.85 *(70.54)*		1.93 *(85.04)*	
28 RE	0.78 *(6.05)*	0.80 *(6.31)*	0.73 *(5.33)*	0.85 *(7.08)*	1.99 *(98.48)*	2.00 *(100.00)*	**2.41** ***(259.50)***	2.38 *(239.88)*
28 LE	0.56 *(3.64)*		0.46 *(2.89)*		1.98 *(95.78)*		1.96 *(91.67)*	
76 RE	0.28 *(1.92)*	0.73 *(5.37)*	0.37 *(2.37)*	0.80 *(6.31)*	1.74 *(55.10)*	2.00 *(100.00)*	1.96 *(90.81)*	2.32 *(208.93)*
76 LE	0.41 *(2.60)*		0.52 *(3.34)*		1.82 *(66.56)*		1.87 *(73.62)*	
323 RE	0.71 *(5.18)*	0.95 *(8.91)*	0.78 *(6.08)*	0.97 *(9.33)*	**2.00** ***(98.93)***	2.00 *(100.00)*	2.28 *(188.89)*	2.54 *(346.74)*
323 LE	0.66 *(4.60)*		0.77 *(5.88)*		**2.00** ***(99.27)***		2.24 *(172.60)*	
372 RE	0.70 *(4.96)*	0.86 *(7.24)*	0.73 *(5.36)*	0.90 *(7.94)*	**2.00** ***(99.63)***	2.00 *(100.00)*	2.30 *(197.81)*	2.45 *(281.84)*
372 LE	0.68 *(4.77)*		0.63 *(4.27)*		1.99 *(98.40)*		2.15 *(142.77)*	
Hyperlipidemia								
10 RE	0.32 *(2.08)*	0.70 *(5.01)*	0.43 *(2.69)*	0.78 *(6.03)*	1.73 *(53.17)*	2.00 *(100.00)*	1.95 *(89.80)*	2.29 *(194.98)*
10 LE	0.34 *(2.18)*		0.29 *(1.94)*		1.75 *(56.69)*		1.93 *(85.05)*	
105 RE	0.22 *(1.65)*	0.60 *(3.98)*	0.36 *(2.27)*	0.69 *(4.90)*	1.74 *(54.39)*	2.00 *(100.00)*	1.91 *(80.58)*	2.20 *(158.49)*
105 LE	0.34 *(2.17)*		0.34 *(2.19)*		1.72 *(52.41)*		1.80 *(63.77)*	
190 RE	0.50 *(3.18)*	0.69 *(4.90)*	0.50 *(3.17)*	0.76 *(5.75)*	1.99 *(98.42)*	2.00 *(100.00)*	2.09 *(123.52)*	2.28 *(190.55)*
190 LE	**0.72** ***(5.26)***		0.67 *(4.71)*		1.99 *(98.74)*		2.26 *(183.16)*	
194 RE	0.42 *(2.66)*	0.80 *(6.31)*	0.55 *(3.58)*	0.86 *(7.24)*	1.98 *(94.60)*	2.00 *(100.00)*	2.02 *(104.04)*	2.39 *(245.47)*
194 LE	0.48 *(2.99)*		0.49 *(3.06)*		1.88 *(75.26)*		2.06 *(115.13)*	
303 RE	0.33 *(2.16)*	0.70 *(5.01)*	0.35 *(2.24)*	0.77 *(5.89)*	1.84 *(69.12)*	2.00 *(100.00)*	1.72 *(52.67)*	2.29 *(194.98)*
303 LE	0.45 *(2.81)*		0.50 *(3.14)*		1.86 *(73.26)*		1.93 *(85.76)*	
320 RE	**0.82** ***(6.63)***	0.72 *(5.25)*	**0.81** ***(6.41)***	0.79 *(6.17)*	**2.00** ***(99.24)***	2.00 *(100.00)*	2.28 *(190.89)*	2.31 *(204.17)*
320 LE	**0.82** ***(6.67)***		**0.79** ***(6.20)***		**2.00** ***(99.53)***		2.21 *(163.69)*	

Table 7.3 (Continued)

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Hyperlipidemia								
370 RE	0.64 *(4.37)*	0.76 *(5.75)*	0.71 *(5.14)*	0.83 *(6.76)*	**2.00 *(99.42)***	2.00 *(100.00)*	2.04 *(110.69)*	2.35 *(223.87)*
370 LE	0.44 *(2.78)*		0.57 *(3.73)*		1.95 *(88.43)*		1.98 *(94.87)*	
Cardiovascular Disease								
246 RE	0.49 *(3.06)*	0.70 *(5.01)*	0.68 *(4.75)*	0.77 *(5.89)*	1.91 *(81.94)*	2.00 *(100.00)*	2.04 *(109.59)*	2.29 *(194.98)*
246 LE	0.45 *(2.79)*		0.56 *(3.64)*		1.99 *(98.50)*		2.08 *(119.28)*	
368 RE	0.84 *(6.94)*	0.97 *(9.33)*	0.82 *(6.55)*	0.96 *(9.12)*	**2.00 *(99.64)***	2.00 *(100.00)*	2.32 *(208.16)*	2.57 *(371.54)*
368 LE	0.92 *(8.25)*		**1.01 *(10.12)***		**2.00 *(100.00)***		**2.43 *(268.93)***	
371 RE	0.32 *(2.10)*	0.74 *(5.50)*	0.47 *(2.97)*	0.81 *(6.46)*	1.93 *(84.34)*	2.00 *(100.00)*	1.92 *(82.28)*	2.33 *(213.80)*
371 LE	0.42 *(2.63)*		0.44 *(2.75)*		1.98 *(95.49)*		1.92 *(84.12)*	
376 RE	0.64 *(4.38)*	0.79 *(6.17)*	0.63 *(4.22)*	0.85 *(7.08)*	**2.0 *(99.28)***	2.00 *(100.00)*	2.17 *(147.28)*	2.38 *(239.88)*
376 LE	0.43 *(2.70)*		0.50 *(3.18)*		1.90 *(79.24)*		1.99 *(97.72)*	

Table 7.3 Mesopic VA thresholds in logMAR and mesopic FCS thresholds in log (% contrast) of participants with systemic vascular disorders. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.3. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

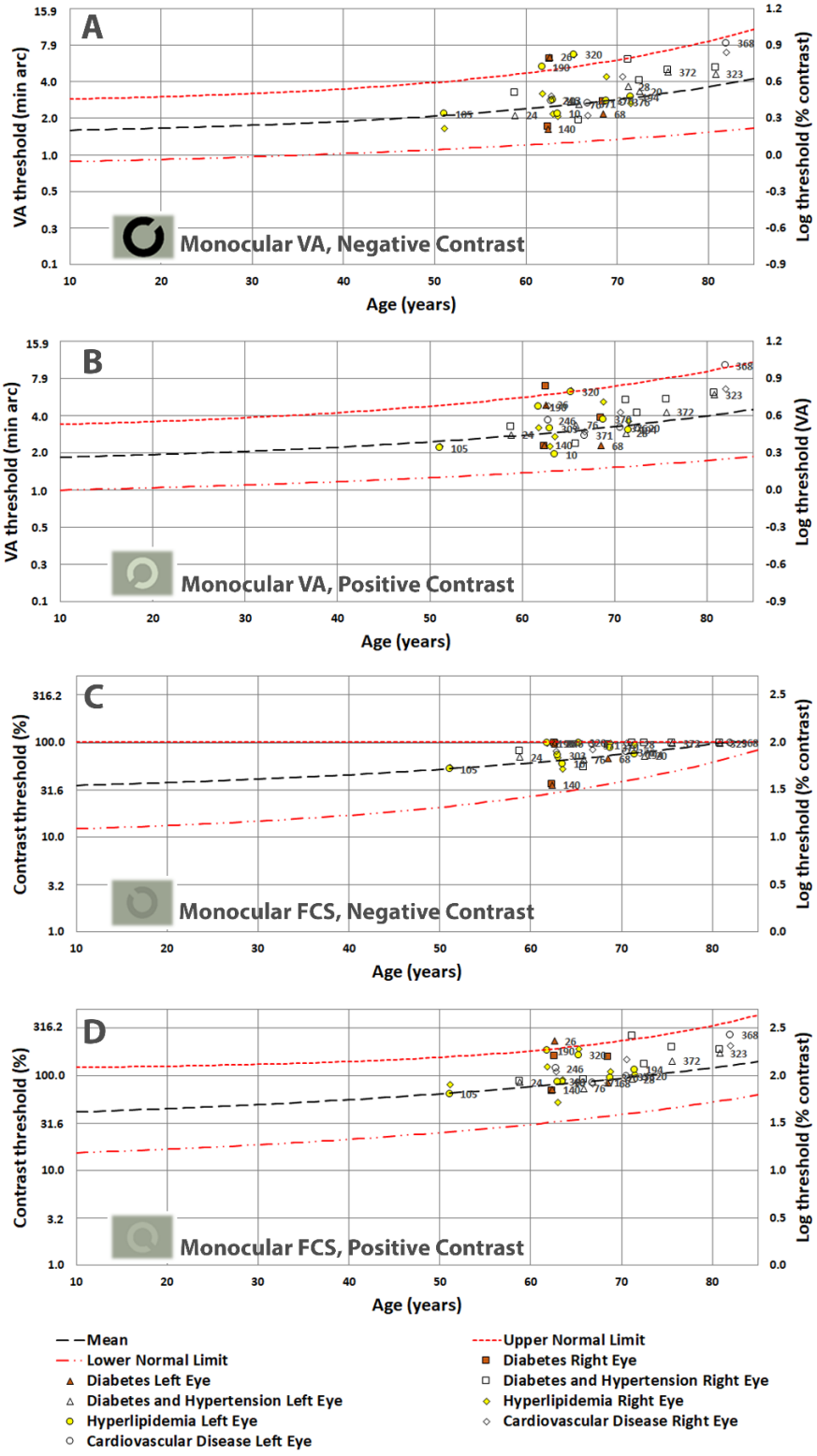


Figure 7.3 (A- D) Mesopic monocular (right and left eye data) VA thresholds in logMar units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with vascular systemic conditions plotted with the means, upper normal limits and lower normal limits based on the results of participants with normal visual performance. The graphs show the results of mesopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.7.2 Non-vascular conditions

Threshold outside the normal upper limit was found for mesopic positive contrast VA measurements in the right eye of one participant with rheumatoid arthritis. In the same participant the right eye positive contrast FCS threshold was borderline. Allergic rhinitis, asthma, hypothyroidism and hyperthyroidism were not related with abnormal thresholds in mesopic conditions. Two participants with epilepsy were tested and one showed higher (abnormal) thresholds in the right eye for mesopic VA measurements in both contrast polarities, and positive contrast FCS. The negative contrast FCS threshold was borderline in the same eye. One participant with ADHD showed mesopic negative contrast VA and positive contrast FCS thresholds for the right eye, and positive contrast VA thresholds in both eyes outside the normal limits. A borderline threshold was found in the right eye for negative contrast FCS. Participants with ulcerative colitis and multiple sclerosis, had thresholds within the normal limits. Thresholds of the four mesopic measurements for each individual are shown in table 7.4 and plotted in figure 7.4 (A-D).

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Rheumatoid Arthritis								
61 RE	0.53 *(3.38)*	0.57 *(3.72)*	**0.70 *(5.01)***	0.65 *(4.47)*	1.98 *(95.36)*	2.00 *(100.00)*	**2.17 *(147.57)***	2.17 *(147.91)*
61 LE	0.40 *(2.50)*		0.48 *(2.99)*		1.63 *(42.99)*		1.87 *(74.60)*	
213 RE	0.24 *(1.74)*	0.52 *(3.31)*	0.27 *(1.85)*	0.60 *(3.98)*	1.75 *(56.32)*	2.00 *(100.00)*	1.69 *(49.09)*	2.13 *(134.90)*
213 LE	0.33 *(2.12)*		0.33 *(2.15)*		1.80 *(62.59)*		1.77 *(59.20)*	
237 RE	0.15 *(1.42)*	0.54 *(3.47)*	0.28 *(1.89)*	0.63 *(4.27)*	1.40 *(24.84)*	2.00 *(100.00)*	1.34 *(21.79)*	2.15 *(141.25)*
237 LE	0.20 *(1.57)*		0.31 *(2.03)*		1.50 *(31.98)*		1.64 *(43.94)*	
259 RE	0.17 *(1.48)*	0.56 *(3.63)*	0.31 *(2.03)*	0.64 *(4.37)*	1.60 *(39.58)*	2.00 *(100.00)*	1.62 *(41.86)*	2.16 *(144.54)*
259 LE	0.27 *(1.85)*		0.20 *(1.59)*		1.64 *(44.06)*		1.59 *(39.25)*	
Allergic Rhinitis								
109 RE	0.29 *(1.97)*	0.57 *(3.72)*	0.30 *(2.01)*	0.66 *(4.57)*	1.62 *(41.37)*	2.00 *(100.00)*	1.68 *(48.11)*	2.18 *(151.36)*
109 LE	0.21 *(1.63)*		0.29 *(1.96)*		1.67 *(46.96)*		1.78 *(60.54)*	
215 RE	0.22 *(1.65)*	0.51 *(3.24)*	0.29 *(1.93)*	0.59 *(3.89)*	1.50 *(31.57)*	2.00 *(100.00)*	1.51 *(32.16)*	2.12 *(131.83)*
215 LE	0.28 *(1.89)*		0.27 *(1.88)*		1.60 *(40.24)*		1.73 *(54.15)*	
255 RE	0.39 *(2.45)*	0.53 *(3.39)*	0.44 *(2.74)*	0.61 *(4.07)*	1.90 *(79.54)*	2.00 *(100.00)*	2.01 *(101.41)*	2.14 *(138.04)*
255 LE	0.50 *(3.19)*		0.53 *(3.41)*		1.94 *(86.81)*		1.93 *(86.06)*	
Asthma								
119 RE	0.43 *(2.71)*	*0.73 (5.37)*	0.47 *(2.97)*	0.80 *(6.31)*	1.91 *(81.15)*	2.00 *(100.00)*	1.83 *(67.75)*	2.32 *(208.93)*
119 LE	0.40 *(2.49)*		0.51 *(3.27)*		1.91 *(80.57)*		1.98 *(96.13)*	
154 RE	0.36 *(2.28)*	0.46 *(2.88)*	*0.37 (2.36)*	0.53 *(3.39)*	1.81 *(64.35)*	2.00 *(100.00)*	1.90 *(80.20)*	2.09 *(123.03)*
154 LE	0.28 *(1.89)*		0.33 *(2.12)*		1.83 *(67.42)*		1.98 *(94.91)*	
185 RE	0.12 *(1.32)*	0.64 *(4.37)*	0.34 *(2.20)*	0.72 *(5.25)*	1.74 *(54.87)*	2.00 *(100.00)*	1.66 *(45.39)*	2.23 *(169.82)*
185 LE	0.52 *(3.30)*		0.62 *(4.20)*		1.98 *(96.00)*		2.03 *(107.00)*	
270 RE	0.24 *(1.74)*	0.60 *(3.98)*	0.28 *(1.92)*	0.69 *(4.90)*	1.54 *(34.61)*	2.00 *(100.00)*	1.70 *(50.20)*	2.20 *(158.49)*
270 LE	0.25 *(1.76)*		*0.28 (1.89)*		1.50 *(31.92)*		1.73 *(54.20)*	
Other Systemic Conditions								
Hypothyroidism								
62 RE	0.17 *(1.49)*	0.51 *(3.24)*	0.20 *(1.59)*	0.60 *(3.98)*	1.49 *(30.90)*	2.00 *(100.00)*	1.60 *(39.81)*	2.13 *(134.90)*
62 LE	0.31 *(2.04)*		0.33 *(2.15)*		1.74 *(55.55)*		1.85 *(70.42)*	
304 RE	0.37 *(2.35)*	0.61 *(4.07)*	0.29 *(1.97)*	0.69 *(4.90)*	1.87 *(74.34)*	2.00 *(100.00)*	1.79 *(65.25)*	2.21 *(162.18)*
304 LE	0.45 *(2.84)*		0.55 *(3.55)*		1.93 *(85.77)*		2.09 *(121.73)*	
Hyperthyroidism								
153 RE	0.48 *(2.99)*	0.80 *(6.31)*	0.73 *(5.33)*	0.85 *(7.08)*	1.99 *(97.14)*	2.00 *(100.00)*	2.25 *(179.88)*	2.38 *(239.88)*
153 LE	*0.36 (2.31)*		0.58 *(3.84)*		1.76 *(57.50)*		1.94 *(87.74)*	
340 RE	0.49 *(3.07)*	0.69 *(4.90)*	0.52 *(3.34)*	0.77 *(5.89)*	1.99 *(97.54)*	2.00 *(100.00)*	2.01 *(102.21)*	2.28 *(190.55)*
340 LE	0.48 *(3.04)*		0.47 *(2.97)*		1.85 *(70.76)*		1.91 *(81.11)*	

Table 7.4 (Continued)

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Hyperthyroidism								
356 RE	0.47 *(2.95)*	0.95 *(8.91)*	0.58 *(3.77)*	0.97 *(9.33)*	1.99 *(97.15)*	2.00 (100.00)	1.99 *(96.84)*	2.55 *(354.81)*
356 LE	0.48 *(2.99)*		0.53 *(3.36)*		1.93 *(84.51)*		1.90 *(80.18)*	
Epilepsy								
77 RE	0.19 *(1.55)*	0.57 *(3.72)*	0.43 *(2.69)*	0.66 *(4.57)*	1.65 *(44.74)*	2.00 (100.00)	1.71 *(51.32)*	2.17 *(147.91)*
77 LE	0.29 *(1.96)*		0.40 *(2.49)*		1.56 *(35.98)*		1.68 *(47.79)*	
296 RE	**0.58 *(3.77)***	0.57 *(3.72)*	**0.70 *(4.99)***	0.66 *(4.57)*	**2.00 *(99.52)***	2.00 (100.00)	**2.32 *(208.81)***	2.18 *(151.36)*
296 LE	0.46 *(2.90)*		0.53 *(3.40)*		1.99 *(98.35)*		191 *(80.69)*	
Multiple Sclerosis								
329 RE	0.26 *(1.81)*	0.65 *(4.47)*	0.34 *(2.20)*	0.73 *(5.37)*	1.67 *(47.05)*	2.00 *(100.00)*	1.75 *(56.84)*	2.24 *(173.78)*
329 LE	0.25 *(1.78)*		0.31 *(2.06)*		1.70 *(49.75)*		1.85 *(71.52)*	
Ulcerative Colitis								
170 RE	0.24 *(1.72)*	0.51 *(3.24)*	0.26 *(1.80)*	0.59 *(3.89)*	1.60 *(39.42)*	2.00 *(100.00)*	1.79 *(61.25)*	2.13 *(134.90)*
170 LE	0.20 *(1.60)*		0.23 *(1.70)*		1.36 *(23.05)*		1.47 *(29.23)*	
Attention deficit hyperactivity disorder								
146 RE	**0.59 *(3.90)***	0.47 *(2.95)*	**0.64 *(4.33)***	0.54 *(3.47)*	**2.00 *(99.32)***	2.00 *(100.00)*	**2.12 *(130.68)***	2.09 *(123.03)*
146 LE	0.46 *(2.89)*		**0.64 *(4.38)***		1.99 *(98.77)*		2.06 *(113.87)*	
252 RE	0.32 *(2.11)*	0.50 *(3.16)*	0.45 *(2.84)*	0.58 *(3.80)*	1.82 *(66.03)*	2.00 *(100.00)*	1.97 *(93.37)*	2.12 *(131.83)*
252 LE	0.30 *(1.99)*		0.31 *(2.06)*		1.57 *(37.38)*		1.66 *(46.00)*	

Table 7.4 Mesopic VA thresholds in logMAR and mesopic FCS thresholds in log (% contrast) of participants with systemic non-vascular disorders. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.4. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

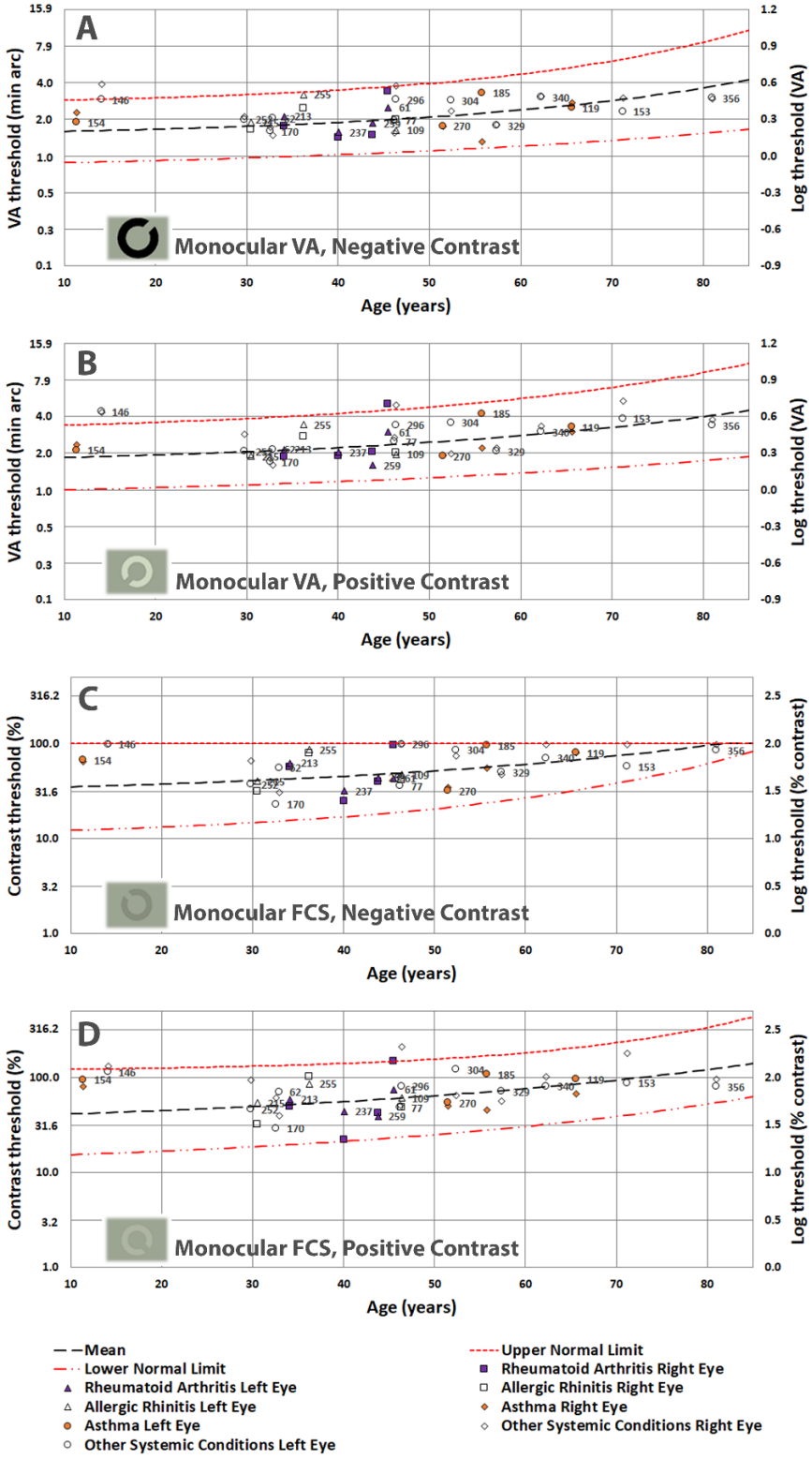


Figure 7.4 (A-D) Mesopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with non-vascular systemic conditions plotted with the means, upper normal limits and lower normal limits based on the results of participants with normal visual performance. The graphs show the results of mesopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.8 Effect of ocular disease on Photopic Visual Acuity and Functional Contrast Sensitivity Function

In this section photopic VA and FCS results of participants with ocular conditions will be described. The conditions consisted of congenital and acquired ocular conditions and anatomical changes caused by refractive laser surgery and orthokeratology.

7.8.1 Fundus abnormalities

Fundus abnormalities can cause substantial changes to photopic VA and FCS (Petzold and Plant, 2006; Bittner and Ferraz, 2020; Puell et al., 2012; Puell, Palomo-Álvarez and Pérez-Carrasco, 2018). However, the amount of change largely depends on the location and severity of the condition. The fundus abnormalities present in the current study were subdivided into the following: macular degeneration (3), hyper- and hypopigmentation (3), glaucoma (5), Best vitelliform macular dystrophy (1), central serous retinopathy (1), macular pucker (1), ablatio retinae (3), macular exudates (1) and Roth spot (1). In table 7.5 participants with fundus abnormalities are listed with the photopic VA and FCS results. The normal upper limits corresponding with the age of each individual are also shown for all measurements in table 7.5. Figure 7.5 (A-D) shows the thresholds of the different measurements with the means, upper normal limits and lower normal limits based on participants with normal visual performance. Results from participants with AMD demonstrated that eyes can be affected differently. This is strongly dependent on the stage/classification of the macular degeneration (Kleiner et al., 1988; Shah et al., 2016). Because of the small number of participants, the macular degeneration was not classified in this study. One of the three participants with AMD exceeded the upper normal limits with the right eye for the photopic negative contrast VA, positive contrast VA and positive contrast FCS measurements. The right eye result of photopic negative contrast FCS was borderline. All the results of the left eye were within the normal range. None of the participants with hyper- and hypopigmentation in the macular area showed photopic VA and FCS thresholds outside the normal limits. However, some of the thresholds were very close to the upper normal limit. The two participants with hyper- and hypopigmentation in both eyes were invited for a follow up after three years. Both participants developed severe AMD, with increased thresholds or unable to perform the measurements. One participant with more advanced glaucoma had thresholds outside the normal limits for photopic negative contrast VA and positive contrast VA in the left eye, and photopic negative contrast FCS in both eyes. The VA and FCS thresholds of the participant with Best vitelliform macular dystrophy were all outside the normal limits in the left eye. In the

right eye photopic positive contrast VA and FCS were outside the normal limits. The participant with a history of central serous retinopathy and the participant with macula pucker did not show abnormal photopic VA and FCS thresholds. One participant with a history of ablatio retinae was not able to perform the test for the affected eye due to poor visual performance. The participant with a history of ablatio retinae in both eyes showed thresholds within the normal limits for all measurements. Macular star (exudates) strongly increases photopic VA and FCS thresholds, which can be explained by the central location of the disease. The Roth spot was more peripheral, and the results of this participant showed that thresholds were not higher in the affected eye than in the fellow eye.

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Fundus Abnormalities: Macular Degeneration								
78 RE	**1.06** ***(11.36)***	0.56 *(3.63)*	**1.18** ***(15.31)***	0.57 *(3.72)*	**2.00** ***(100.00)***	2.00 *(100.00)*	**2.20** ***(156.82)***	2.14 *(138.04)*
78 LE	0.26 *(1.81)*		0.36 *(2.28)*		1.52 *(33.29)*		1.61 *(40.99)*	
196 RE	0.42 *(2.66)*	0.64 *(4.37)*	0.42 *(2.64)*	0.62 *(4.17)*	1.79 *(62.39)*	2.00 *(100.00)*	1.57 *(37.07)*	2.35 *(223.87)*
196 LE	0.49 *(3.07)*		0.34 *(2.17)*		1.87 *(74.09)*		1.87 *(74.09)*	
324 RE	0.27 *(1.87)*	0.53 *(3.39)*	0.36 *(2.31)*	0.55 *(3.55)*	1.59 *(39.08)*	1.98 *(95.50)*	1.71 *(51.65)*	2.06 *(114.82)*
324 LE	0.19 *(1.56)*		0.18 *(1.50)*		1.37 *(23.28)*		1.38 *(23.81)*	
Hyper- and hypopigmentation both eyes								
23 RE	0.24 *(1.73)*	0.46 *(2.88)*	*0.42* *(2.61)*	*0.50* *(3.16)*	1.57 *(37.07)*	1.85 *(70.79)*	1.60 *(39.55)*	1.89 *(77.62)*
23 LE	0.45 *(2.80)*		0.43 *(2.70)*		1.78 *(60.47)*		1.62 *(41.86)*	
128 RE	0.29 *(1.93)*	0.46 *(2.88)*	0.33 *(2.12)*	0.50 *(3.16)*	1.59 *(38.51)*	1.85 *(70.79)*	1.57 *(37.51)*	1.89 *(77.62)*
128 LE	0.44 *(2.73)*		0.41 *(2.56)*		1.68 *(47.82)*		1.79 *(61.60)*	
Hyper- and hypopigmentation right eye								
52 RE	0.20 *(1.58)*	0.38 *(2.40)*	0.18 *(1.52)*	0.42 *(2.63)*	1.50 *(31.98)*	1.68 *(47.86)*	1.51 *(32.64)*	1.72 *(52.48)*
52 LE	0.14 *(1.39)*		0.22 *(1.67)*		1.23 *(16.98)*		1.23 *(16.82)*	
Glaucoma								
56 RE	0.00 *(1.01)*	0.44 *(2.75)*	0.10 *(1.26)*	0.47 *(2.95)*	1.44 *(27.34)*	1.80 *(63.10)*	1.40 *(25.16)*	1.83 *(67.61)*
56 LE	0.07 *(1.18)*		-0.03 *(0.93)*		1.21 *(16.26)*		1.14 *(13.79)*	
97 RE	0.23 *(1.69)*	0.41 *(2.57)*	0.26 *(1.83)*	0.45 *(2.82)*	1.58 *(37.79)*	1.75 *(56.23)*	1.58 *(37.98)*	1.79 *(61.66)*
97 LE	0.22 *(1.66)*		0.20 *(1.59)*		1.28 *(19.07)*		1.15 *(13.98)*	
181 RE	0.44 *(2.75)*	0.48 *(3.02)*	0.47 *(2.92)*	0.51 *(3.24)*	**1.92** ***(82.42)***	1.88 *(75.86)*	1.76 *(57.19)*	1.93 *(85.11)*
181 LE	**1.17** ***(14.94)***		***1.18*** ***(14.97)***		**2.00** ***(99.54)***		1.92 *(82.76)*	

Table 7.5 (Continued)

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Glaucoma								
273 RE	0.11 *(1.28)*	0.45 *(2.82)*	0.33 *(2.14)*	0.49 *(3.09)*	1.46 *(28.75)*	1.83 *(67.61)*	1.61 *(40.71)*	1.86 *(72.44)*
273 LE	0.21 *(1.61)*		0.32 *(2.09)*		1.61 *(40.81)*		1.58 *(38.23)*	
361 RE	0.44 *(2.76)*	0.45 *(2.82)*	**0.54 *(3.49)***	0.49 *(3.09)*	**1.93 *(85.26)***	1.83 *(67.61)*	**1.90 *(79.97)***	1.87 *(74.13)*
361 LE	0.24 *(1.75)*		0.37 *(2.33)*		1.55 *(35.91)*		1.49 *(31.22)*	
Best Vitelliform Macular Dystrophy								
2 RE	0.24 *(1.73)*	0.31 *(2.04)*	**0.35 *(2.26)***	0.35 *(2.24)*	1.48 *(30.41)*	1.54 *(34.67)*	**1.76 *(57.30)***	1.60 *(39.81)*
2 LE	**0.58 *(3.78)***		**0.87 *(7.37)***		**1.98 *(95.25)***		**2.15 *(142.81)***	
Central Serous Retinopathy History left eye								
127 RE	0.16 *(1.43)*	0.32 *(2.09)*	0.13 *(1.36)*	0.36 *(2.29)*	1.37 *(23.59)*	1.55 *(35.48)*	1.41 (25.48)	1.61 *(40.74)*
127 LE	0.18 *(1.52)*		0.11 *(1.28)*		1.16 *(14.53)*		1.25 *(17.80)*	
Macular Pucker left eye								
211 RE	0.25 *(1.78)*	0.44 *(2.75)*	0.23 *(1.69)*	0.48 *(3.02)*	1.33 *(21.26)*	1.81 *(64.57)*	1.47 (29.23)	1.85 *(70.79)*
211 LE	0.36 *(2.28)*		0.41 *(2.56)*		1.56 *(36.46)*		1.54 *(34.40)*	
Ablatio Retinae history both eyes								
291 RE	0.14 *(1.39)*	0.39 *(2.45)*	0.32 *(2.10)*	0.43 *(2.69)*	1.25 *(17.84)*	1.71 *(51.29)*	1.33 (21.14)	1.74 *(54.95)*
291 LE	0.16 *(1.46)*		0.10 *(1.26)*		1.59 *(38.83)*		1.48 *(29.87)*	
Ablatio Retinae history right eye								
266 RE	-	0.37 *(2.34)*	-	0.41 *(2.57)*	-	1.66 *(45.71)*	-	1.70 *(50.12)*
266 LE	0.23 *(1.71)*		**0.47 *(2.96)***		**1.67 *(47.06)***		**1.93 *(84.67)***	
Macular Star (Exudates) left eye								
129 RE	0.36 *(2.31)*	0.44 *(2.75)*	0.29 *(1.94)*	0.47 *(2.95)*	1.71 *(51.35)*	1.80 *(63.10)*	1.81 (64.23)	1.84 *(69.18)*
129 LE	**0.79 *(6.17)***		**0.77 *(5.88)***		**2.00 *(99.56)***		**2.33 *(214.11)***	
Roth Spot left eye								
88 RE	**0.37 *(2.37)***	0.33 *(2.14)*	**0.43 *(2.69)***	0.37 *(2.34)*	1.55 *(35.66)*	1.58 *(38.02)*	**1.71 (51.46)**	1.63 *(42.66)*
88 LE	0.12 *(1.33)*		0.31 *(2.04)*		1.29 *(19.56)*		1.45 *(28.04)*	

Table 7.5 Photopic VA thresholds in logMAR and photopic FCS thresholds in log (% contrast) of participants with fundus abnormalities. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.5. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

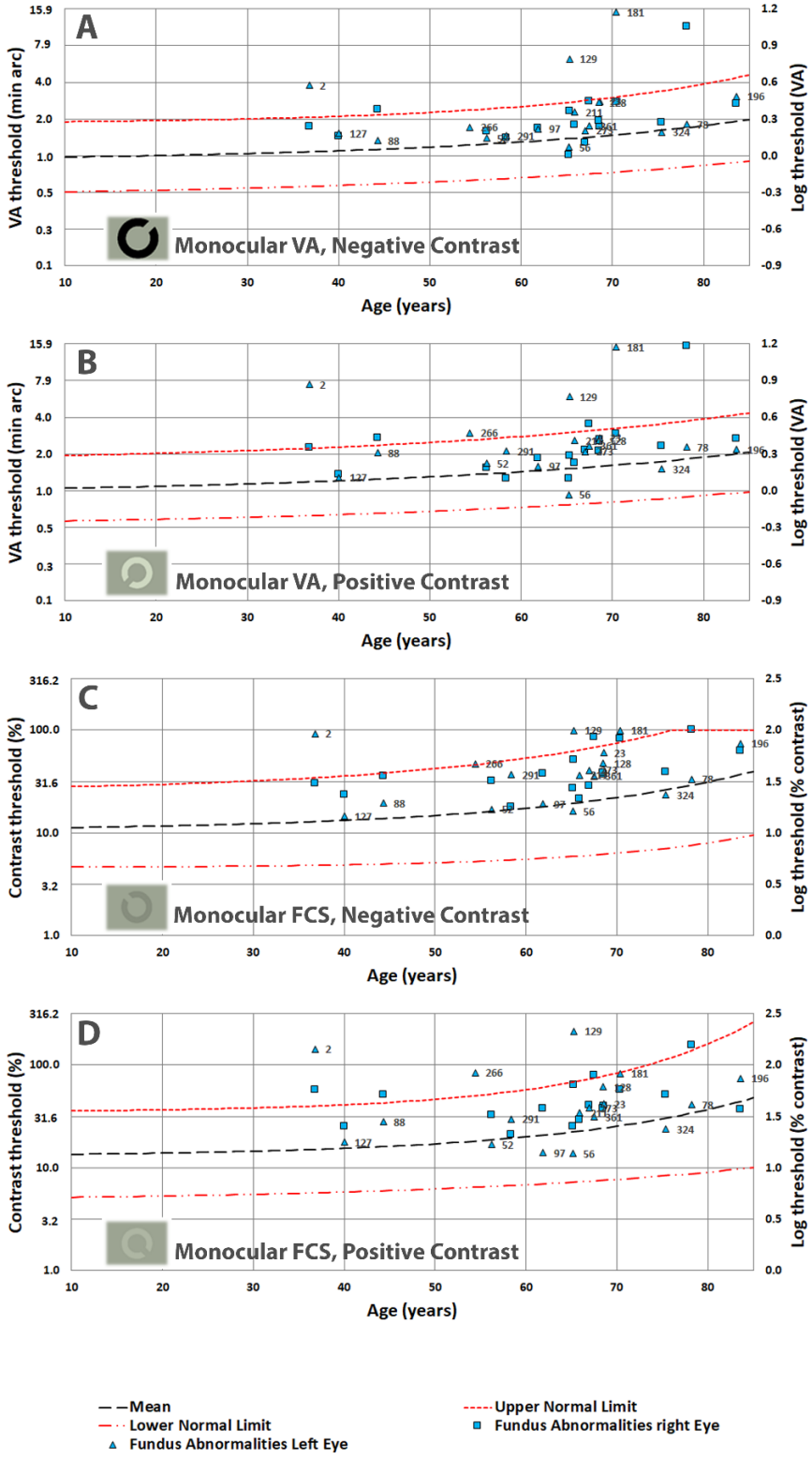


Figure 7.5 (A-D) Photopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with fundus abnormalities plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of photopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.8.2 Amblyopia

Table 7.6 shows the photopic VA and FCS results of participants with amblyopic eyes. The participants were divided into amblyopia right eye and amblyopia left eye. As expected, most thresholds of the amblyopic eyes exceeded upper normal limits for all photopic measurements. Three participants could not perform the Acuity-*Plus* test with their amblyopic eye. The thresholds of the amblyopic and contralateral eyes are plotted in figure 7.6 (A-D). The numbers of participants corresponding to table 7.6, are on the right side of the left eye results. The figure also illustrates how the thresholds are compared to the means, upper normal limits and lower normal limits of participants with normal visual performance.

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Amblyopia: Amblyopia right eye								
39 RE	**0.34** ***(2.18)***	0.28 *(1.91)*	**0.44** ***(2.74)***	0.29 *(1.95)*	1.42 *(26.53)*	1.46 *(28.84)*	**1.63** ***(42.20)***	1.56 *(36.31)*
39 LE	0.22 *(1.65)*		**0.33** ***(2.12)***		1.29 *(19.55)*		1.52 *(33.48)*	
169 RE	0.19 *(1.55)*	0.37 *(2.34)*	0.17 *(1.49)*	0.41 *(2.57)*	1.49 *(30.79)*	1.65 *(44.67)*	1.48 *(29.96)*	1.69 *(48.98)*
169 LE	0.10 *(1.27)*		0.08 *(1.21)*		1.31 *(20.35)*		1.16 *(14.48)*	
264 RE	0.29 *(1.95)*	0.33 *(2.14)*	0.29 *(1.97)*	0.37 *(2.34)*	**1.81** ***(64.80)***	1.57 *(37.15)*	1.56 *(36.29)*	1.62 *(41.69)*
264 LE	0.19 *(1.54)*		0.20 *(1.60)*		1.30 *(20.11)*		1.28 *(19.15)*	
300 RE	-	0.36 *(2.29)*	-	0.40 *(2.51)*	-	1.63 *(42.66)*	-	1.67 *(46.77)*
300 LE	0.07 *(1.18)*		0.16 *(1.44)*		1.09 *(12.22)*		1.03 *(10.61)*	
309 RE	**0.40** ***(2.52)***	0.28 *(1.91)*	0.29 *(1.94)*	0.30 *(2.00)*	**1.68** ***(48.37)***	1.47 *(29.51)*	1.40 *(24.90)*	1.56 *(36.31)*
309 LE	-0.02 *(0.95)*		0.15 *(1.41)*		1.25 *(17.91)*		1.35 *(22.37)*	
Amblyopia left eye								
70 RE	0.18 *(1.51)*	0.38 *(2.40)*	0.16 *(1.45)*	0.43 *(2.69)*	1.36 *(22.67)*	1.69 *(48.98)*	1.31 *(20.36)*	1.72 *(52.48)*
70 LE	**0.70** ***(5.00)***		**0.84** ***(6.95)***		**2.00** ***(99.63)***		**2.15** ***(141.28)***	
138 RE	0.03 *(1.07)*	0.29 *(1.95)*	0.14 *(1.38)*	0.31 *(2.04)*	1.17 *(14.63)*	1.48 *(30.20)*	1.17 *(14.90)*	1.57 *(37.15)*
138 LE	**0.32** ***(2.08)***		0.26 *(1.83)*		1.23 *(16.96)*		1.36 *(23.16)*	
199 RE	0.17 *(1.47)*	0.35 *(2.24)*	0.21 *(1.64)*	0.39 *(2.45)*	1.32 *(20.75)*	1.62 *(41.69)*	1.32 *(20.66)*	1.66 *(45.71)*
199 LE	**0.53** ***(3.37)***		**0.53** ***(3.36)***		**1.68** ***(47.88)***		**2.13** ***(134.14)***	
201 RE	0.25 *(1.77)*	0.58 *(3.80)*	0.26 *(1.82)*	0.58 *(3.80)*	1.22 *(16.49)*	2.00 *(100.00)*	1.37 *(23.54)*	2.18 *(151.36)*
201 LE	-		-		-		-	
238 RE	0.30 *(1.98)*	0.41 *(2.57)*	0.20 *(1.57)*	0.45 *(2.82)*	1.61 *(41.07)*	1.73 *(53.70)*	1.57 *(36.88)*	1.77 *(58.88)*
238 LE	-		-		-		-	

Table 7.6 (Continued)

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Amblyopia left eye								
272 RE	-0.03 *(0.94)*	0.31 *(2.04)*	0.00 *(1.01)*	0.33 *(2.14)*	1.20 *(15.96)*	1.52 *(33.11)*	1.21 *(16.14)*	1.59 *(38.90)*
272 LE	**0.45 *(2.82)***		**0.58 *(3.80)***		**1.99 *(97.87)***		**2.03 *(107.61)***	
276 RE	0.17 *(1.48)*	0.39 *(2.45)*	0.21 *(1.62)*	0.43 *(2.69)*	1.29 *(19.62)*	1.70 *(50.12)*	1.45 *(28.02)*	1.74 *(54.95)*
276 LE	0.19 *(1.55)*		0.26 *(1.82)*		1.20 *(15.90)*		1.20 *(15.84)*	
287 RE	0.18 *(1.53)*	0.36 *(2.29)*	0.18 *(1.51)*	0.40 *(2.51)*	1.22 *(16.42)*	1.63 *(42.66)*	1.29 *(19.56)*	1.67 *(46.77)*
287 LE	**0.46 *(2.87)***		**0.61 *(4.12)***		**1.96 *(90.79)***		**1.96 *(91.70)***	
313 RE	0.16 *(1.44)*	0.43 *(2.69)*	0.19 *(1.54)*	0.47 *(2.95)*	1.21 *(16.05)*	1.79 *(61.66)*	1.48 *(29.86)*	1.82 *(66.07)*
313 LE	**0.37 *(2.37)***		0.26 *(1.84)*		1.39 *(24.41)*		1.54 *(35.01)*	
362 RE	0.18 *(1.52)*	0.49 *(3.09)*	0.12 *(1.32)*	0.51 *(3.24)*	1.28 *(19.20)*	1.90 *(79.43)*	1.18 *(15.19)*	1.95 *(89.13)*
362 LE	0.43 *(2.72)*		0.42 *(2.66)*		1.50 *(31.81)*		1.64 *(43.76)*	

Table 7.6 Photopic VA thresholds in logMAR and photopic FCS thresholds in log (% contrast) of participants with amblyopia. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.6. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

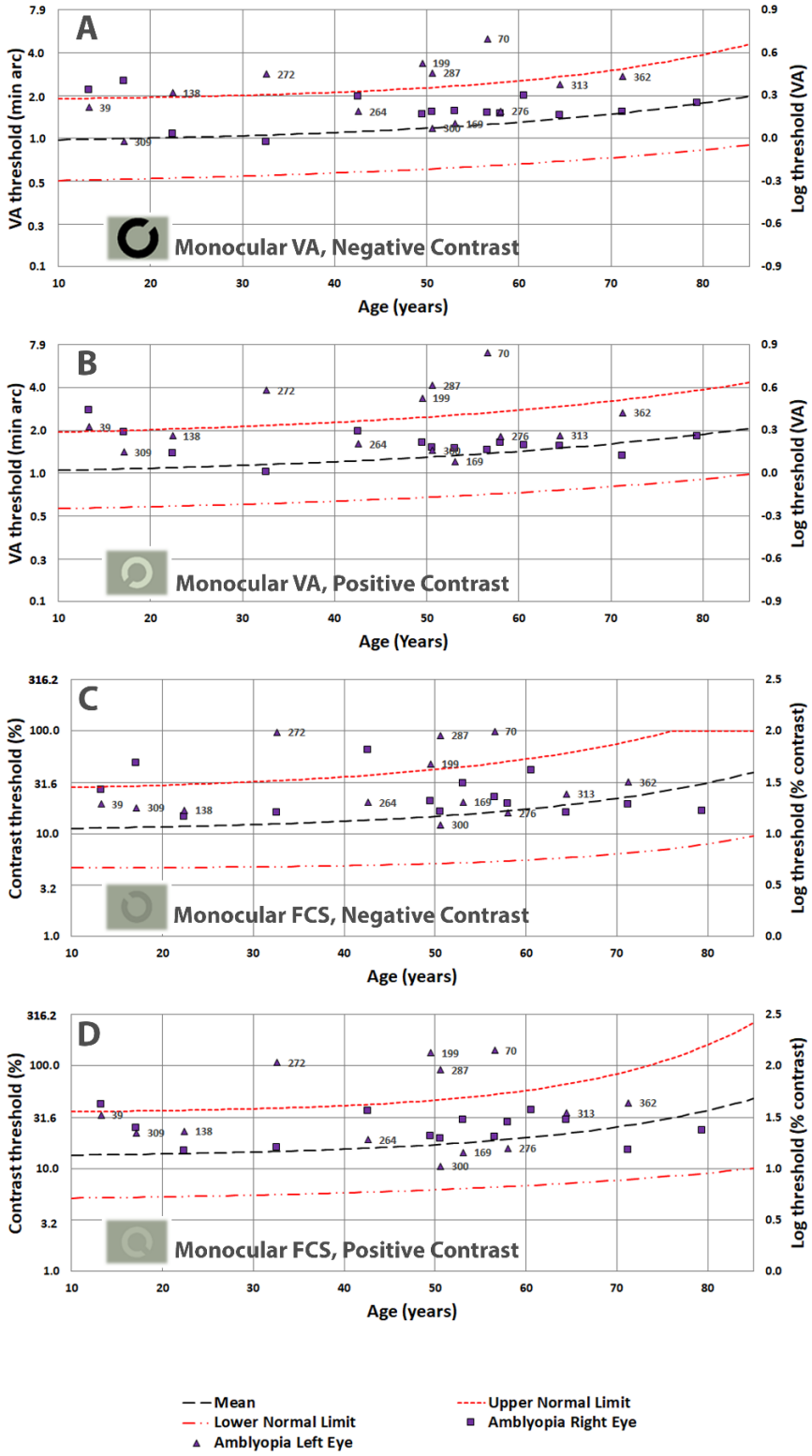


Figure 7.6 (A-D) Photopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with amblyopia plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of photopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.8.3 Anterior segment conditions

The anterior segment conditions group consisted of participants with anterior segment disease, such as congenital lens opacities and keratoconus, and participants with non-pathological corneal changes for refractive error correction by refractive laser surgery or orthokeratology. Table 7.7 shows the VA and FCS results of the different participants within this group. In figure 7.7 (A-D), each individual's VA and FCS results are plotted. Study participants had undergone different methods of refractive laser surgery. Participants 51, 156 and 242 underwent Laser Assisted Subepithelial Keratectomy (LASEK), participants 274, 281, 284, 305 and 306 Laser Assisted In Situ Keratomileusis (LASIK), participant 302 Photo Refractive Keratectomy (PRK) and participant 382 Transepithelial Photo Refractive Keratectomy (Trans PRK). Two participants had thresholds outside the normal limits for photopic measurements. One participant who underwent a LASEK treatment showed an abnormal left eye threshold with photopic positive contrast FCS, while another participant had an abnormal negative contrast VA threshold in the right eye after LASIK. Orthokeratology reshapes the cornea to correct for myopic refractive error using specially designed and fitted contact lenses (Nti and Berntsen, 2020). Orthokeratology lenses are also prescribed in children to reduce myopia progression by slowing axial length elongation (Bullimore and Johnson, 2020). The growth signal is reduced by the hyperopic defocus and peripheral blur in orthokeratology (Hiraoka, 2022). Two participants with orthokeratology performed the test, and both had normal photopic VA and FCS thresholds. In one participant with congenital lens opacities the left eye positive contrast VA was above the normal upper limit. In the more advanced keratoconus right eye of the participant with keratoconus, abnormal FCS in negative positive contrast was found.

Participant	Photopic VA Negative Contrast in logMAR *(MOA)*	Photopic VA Negative Contrast UNL in logMAR *(MOA)*	Photopic VA Positive Contrast in logMAR *(MOA)*	Photopic VA Positive Contrast UNL in logMAR *(MOA)*	Photopic FCS Negative Contrast in log (%) *(PCT)*	Photopic FCS Negative Contrast UNL in log (%) *(PCT)*	Photopic FCS Positive Contrast in log (%) *(PCT)*	Photopic FCS Positive Contrast UNL in log (%) *(PCT)*
Refractive Laser Surgery								
51 RE	-0.06 *(0.87)*	0.33 *(2.14)*	0.15 *(1.42)*	0.36 *(2.29)*	1.13 *(13.60)*	1.56 *(36.31)*	1.23 *(16.99)*	1.62 *(41.69)*
51 LE	0.19 *(1.56)*		0.32 *(2.08)*		1.50 *(31.57)*		**1.69 *(49.06)***	
156 RE	0.00 *(1.00)*	0.33 *(2.14)*	0.14 *(1.37)*	0.37 *(2.34)*	1.08 *(11.95)*	1.58 *(38.02)*	1.12 *(13.33)*	1.63 *(42.66)*
156 LE	0.00 *(0.99)*		-0.03 *(0.94)*		1.13 *(13.47)*		0.91 *(8.05)*	
242 RE	0.04 *(1.10)*	0.32 *(2.09)*	0.09 *(1.22)*	0.35 *(2.24)*	1.18 *(15.06)*	1.55 *(35.48)*	1.18 *(15.24)*	1.61 *(40.74)*
242 LE	0.08 *(1.19)*		0.04 *(1.10)*		1.03 *(10.71)*		1.09 *(12.39)*	
274 RE	0.05 *(1.13)*	0.36 *(2.29)*	0.14 *(1.38)*	0.40 *(2.51)*	1.50 *(31.38)*	1.64 *(43.65)*	1.44 *(27.59)*	1.68 *(47.86)*
274 LE	0.10 *(1.27)*		0.17 *(1.47)*		1.45 *(27.95)*		1.43 *(27.16)*	
281 RE	0.17 *(1.49)*	0.35 *(2.24)*	0.17 *(1.48)*	0.39 *(2.45)*	1.38 *(23.86)*	1.61 *(40.74)*	1.52 *(33.24)*	1.66 *(45.71)*
281 LE	0.05 *(1.11)*		0.19 *(1.56)*		1.36 *(23.10)*		1.45 *(28.10)*	
284 RE	0.19 *(1.54)*	0.36 *(2.29)*	0.20 *(1.58)*	0.40 *(2.51)*	1.09 *(12.26)*	1.63 *(42.66)*	1.38 *(23.99)*	1.67 *(46.77)*
284 LE	0.12 *(1.32)*		0.17 *(1.47)*		1.02 *(10.53)*		1.12 *(13.09)*	
302 RE	0.10 *(1.26)*	0.36 *(2.29)*	0.19 *(1.55)*	0.40 *(2.51)*	1.26 *(18.02)*	1.63 *(42.66)*	1.38 *(24.18)*	1.67 (46.77)
302 LE	0.01 *(1.03)*		0.06 *(1.16)*		1.19 *(13.15)*		1.27 *(18.63)*	
305 RE	0.28 *(1.92)*	0.33 *(2.14)*	0.19 *(1.54)*	0.37 *(2.34)*	1.49 *(30.57)*	1.57 *(37.15)*	1.45 *(28.23)*	1.62 *(41.69)*
305 LE	**0.34 *(2.18)***		0.17 *(1.49)*		1.40 *(25.04)*		1.29 *(19.59)*	
306 RE	0.12 *(1.32)*	0.33 *(2.14)*	0.09 *(1.22)*	0.37 *(2.34)*	1.18 *(14.98)*	1.57 *(37.15)*	1.13 *(13.52)*	1.63 *(42.66)*
306 LE	-0.09 *(0.82)*		0.06 *(1.15)*		1.20 *(15.96)*		1.08 *(12.14)*	
382 RE	0.08 *(1.21)*	0.29 *(1.95)*	0.06 *(1.16)*	0.31 *(2.04)*	0.85 *(7.06)*	1.48 *(30.20)*	1.00 *(9.97)*	1.57 *(37.15)*
382 LE	0.12 *(1.31)*		0.11 *(1.29)*		0.90 *(7.89)*		1.06 *(11.51)*	
Orthokeratology								
155 RE	0.17 *(1.47)*	0.28 *(1.91)*	0.19 *(1.56)*	0.29 *(1.95)*	1.43 *(26.98)*	1.46 *(28.84)*	1.38 *(23.94)*	1.56 *(36.31)*
155 LE	0.10 *(1.25)*		0.13 *(1.34)*		1.10 *(12.37)*		1.30 *(19.82)*	
212 RE	0.19 *(1.55)*	0.32 *(2.09)*	0.05 *(1.11)*	0.35 *(2.24)*	1.35 *(22.58)*	1.48 *(30.20)*	1.44 *(27.50)*	1.61 *(40.74)*
212 LE	0.06 *(1.16)*		0.08 *(1.19)*		1.27 *(18.81)*		1.37 *(23.44)*	
Congenital Lens Opacities								
19 RE	0.16 *(1.44)*	0.28 *(1.91)*	0.10 *(1.25)*	0.30 *(2.00)*	1.35 *(22.32)*	1.46 (28.84)	1.30 *(19.81)*	1.56 *(36.31)*
19 LE	0.05 *(1.13)*		**0.42 *(2.61)***		1.32 *(20.71)*		1.27 *(18.69)*	
192 RE	-0.09 *(0.81)*	0.29 *(1.95)*	-0.01 *(0.97)*	0.31 *(2.04)*	0.91 *(8.13)*	1.48 *(30.20)*	0.93 *(8.48)*	1.57 *(37.15)*
192 LE	0.01 *(1.02)*		-0.02 *(0.95)*		1.07 *(11.82)*		1.12 *(13.07)*	
Keratoconus								
214 RE	0.17 *(1.47)*	0.34 *(2.19)*	0.28 *(1.91)*	0.38 *(2.40)*	1.58 *(37.76)*	1.59 *(38.90)*	**1.67 *(46.28)***	1.64 *(43.65)*
214 LE	0.11 *(1.28)*		0.14 *(1.39)*		1.19 *(15.48)*		1.35 *(22.53)*	

Table 7.7 Photopic VA thresholds in logMAR and photopic FCS thresholds in log (% contrast) of participants with anterior segment conditions. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.7. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

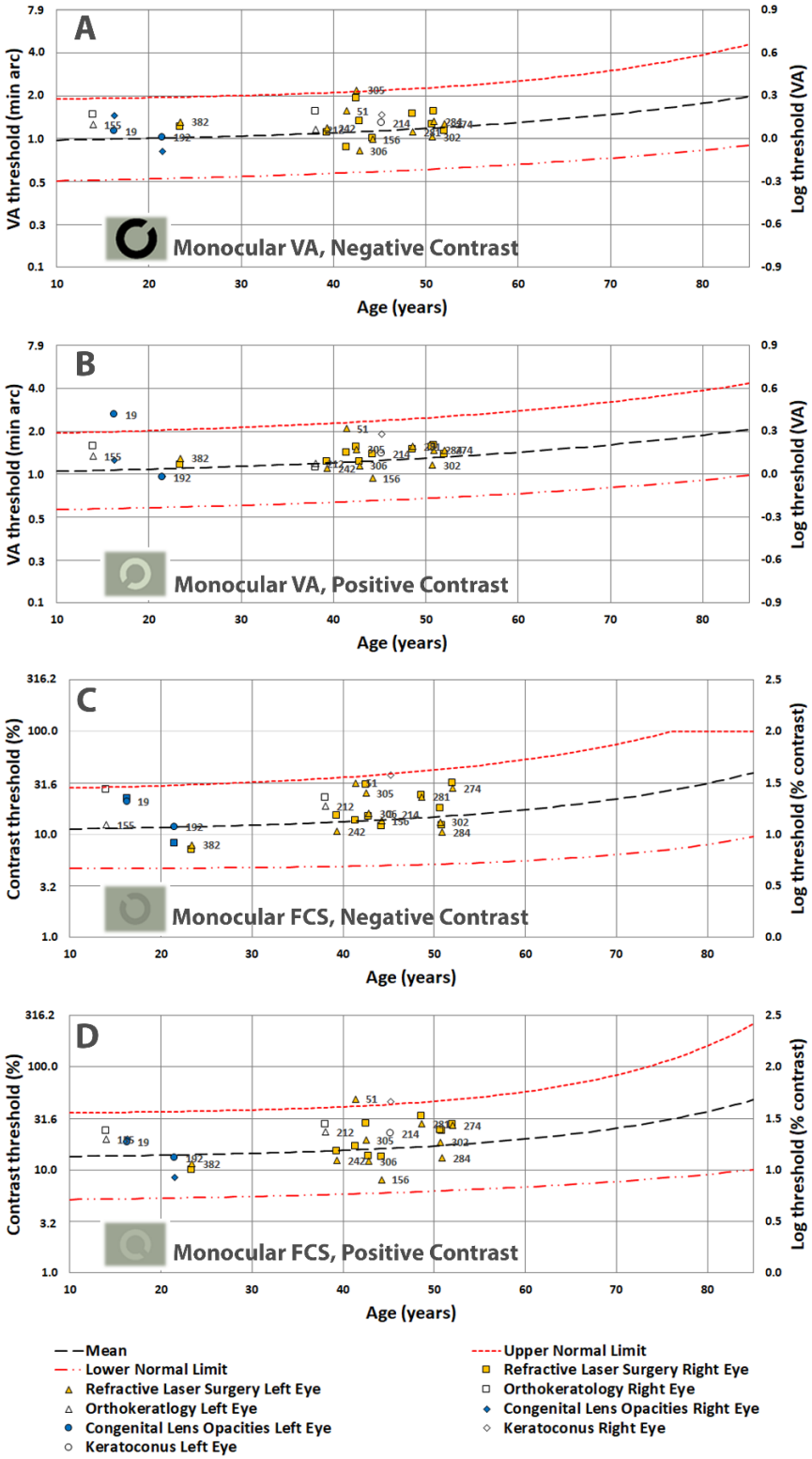


Figure 7.7 (A-D) Photopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with anterior segment conditions plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of photopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.8.4 Lens Opacities

In the current study, only participants with lens gradings of 0, 1 and 2 according to the Optometry Grading Scale were included. Lens gradings of 3, 4 and 5 were excluded. The effects of the lens gradings on spatial vision were assessed in the participants who remained after the selection filters for normal photopic visual performance. The effects of cortical and posterior subcapsular lens opacities were disregarded if the number of participants was too low for reliable statistical analysis. Independent t-tests were conducted for each decade separately to exclude the effect of normal ageing. The independent t-tests were performed for the right and left eye results separately, and with the right or left eye randomised. The Bonferroni correction was applied due to multiple comparisons. In the second and third decade the data allowed for the analysis of the difference between nuclear cataract gradings of 0 and 1, and in the fourth, fifth and sixth decade between nuclear cataract gradings 1 and 2. Higher lens gradings resulted overall in slightly higher VA and FCS thresholds. However, none of the comparisons revealed statistically significant differences between the gradings with the independent t-test (P>0.006).

7.9 The effect of ocular disease on Mesopic Visual Acuity and Functional Contrast Sensitivity

This section will describe the results of mesopic VA and FCS in individuals with ocular conditions. This is of interest if some conditions potentially affect mesopic VA and FCS thresholds more than photopic functions.

7.9.1 Fundus abnormalities

Two of the three participants with AMD showed borderline negative contrast thresholds. However, the participant with extremely high right eye photopic VA and FCS thresholds has not been able to perform the test for the right eye under mesopic conditions due to the advanced stage of the AMD. These results suggest that the thresholds are strongly dependent on the severity of the disease. Furthermore, the remaining negative contrast FCS results were close to the maximum of 2.00 log (100%). Thresholds for one participant with hyper- and hypopigmentation in the macular area were outside the normal limits for both eyes with negative contrast VA and for the left eye with positive contrast VA and positive contrast FCS. The right eye threshold of positive contrast VA was borderline. The negative contrast FCS results can also be considered clinically abnormal with borderline thresholds. The other participant with hyper- and hypopigmentation in

both eyes showed an abnormal positive contrast FCS threshold for the left eye, while negative contrast FCS was borderline. The participant with hyper- and hypopigmentation in the right eye showed thresholds above the upper normal limit with negative contrast VA and positive contrast VA. These results may demonstrate that hyper- and hypopigmentation affect mesopic vision more than photopic. As described in the section on photopic measurements with fundus abnormalities, the two participants with hyper- and hypopigmentation developed AMD within three years. The thresholds were increased in one participant, and the other was unable to perform the test due to decreased visual performance after three years. Three of the five participants suffering from glaucoma showed abnormal or borderline thresholds for at least one of the mesopic measurements. In contrast, the photopic measurements were abnormal in two participants. Mesopic thresholds were not normal or borderline in two glaucoma participants with positive contrast FCS for one eye. Negative and/or positive contrast VA were abnormal for at least one eye in two glaucoma participants, and in four glaucoma participants, negative contrast results were borderline or close to the maximum of 2.00 log (100%). In the participants with glaucoma included in this study, mesopic vision was more affected than photopic. All mesopic measurements were outside the normal limits or borderline in the participant with Best vitelliform macular dystrophy and within the normal range in the participants with a history of central serous retinopathy and macular pucker. A history of ablatio retinae caused an abnormal positive contrast FCS threshold for the left eye of one participant. One participant was unable to perform the test for the eye with a history of ablatio retinae as spatial vision was severely decreased. Most of the mesopic measurements revealed thresholds outside the normal limits or borderline in the affected eye of the participant with a macular star (exudates). The participant with a Roth spot showed normal mesopic thresholds in the affected eye. The contralateral eye showed thresholds outside the normal limits with mesopic negative contrast VA and positive contrast FCS, which may be caused by an unknown underlying condition. The mesopic negative contrast FCS threshold of the contralateral eye was borderline. In table 7.8, all mesopic thresholds of the participants with fundus abnormalities are listed with each individual's corresponding upper normal limits. These thresholds are also plotted in figure 7.8 (A-D), which shows how these points relate to the upper normal limits.

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Fundus Abnormalities: Macular Degeneration								
78 RE	-	0.90 *(7.94)*	-	0.94 *(8.71)*	-	2.00 *(100.00)*	-	2.49 *(309.03)*
78 LE	0.61 *(4.11)*		0.71 *(5.10)*		1.99 *(97.30)*		2.19 *(156.16)*	
196 RE	0.58 *(3.84)*	1.00 *(10.00)*	0.64 *(4.39)*	1.01 *(10.23)*	**2.00 *(99.25)***	2.00 *(100.00)*	2.10 *(126.71)*	2.61 *(407.38)*
196 LE	0.59 *(3.91)*		0.81 *(6.41)*		1.99 *(97.40)*		2.15 *(141.66)*	
324 RE	0.71 *(5.18)*	0.86 *(7.24)*	0.68 *(4.81)*	0.90 *(7.94)*	**2.00 *(99.00)***	2.00 *(100.00)*	2.27 *(185.47)*	2.45 *(281.84)*
324 LE	0.52 *(3.31)*		0.42 *(2.63)*		1.99 *(97.26)*		1.96 *(91.47)*	
Hyper- and hypopigmentation both eyes								
23 RE	0.45 *(2.80)*	0.76 *(5.75)*	0.51 *(3.22)*	0.83 *(6.76)*	1.96 *(91.36)*	2.00 *(100.00)*	2.04 *(109.86)*	2.35 *(223.87)*
23 LE	0.68 *(4.75)*		0.59 *(3.87)*		**2.00 *(99.25)***		**2.42 *(261.50)***	
128 RE	**0.80 *(6.34)***	0.76 *(5.75)*	**0.83 *(6.82)***	0.83 *(6.76)*	**2.00 *(99.68)***	2.00 *(100.00)*	2.28 *(188.43)*	2.35 *(223.87)*
128 LE	**1.29 *(19.45)***		**1.03 *(10.76)***		**2.00 *(99.83)***		**2.50 *(315.62)***	
Hyper- and hypopigmentation right eye								
52 RE	**0.65 *(4.48)***	0.64 *(4.37)*	**0.72 *(5.27)***	0.72 *(5.25)*	1.98 *(96.38)*	2.00 *(100.00)*	2.14 *(138.08)*	2.23 *(169.82)*
52 LE	0.45 *(2.84)*		0.47 *(2.93)*		1.77 *(59.43)*		1.93 *(84.79)*	
Glaucoma								
56 RE	**0.73 *(5.31)***	0.72 *(5.25)*	0.63 *(4.25)*	0.79 *(6.17)*	1.99 *(98.61)*	2.00 *(100.00)*	2.17 *(148.67)*	2.31 *(204.17)*
56 LE	0.38 *(2.39)*		0.51 *(3.24)*		1.95 *(88.61)*		1.97 *(94.22)*	
97 RE	0.29 *(1.97)*	0.69 *(4.90)*	0.41 *(2.60)*	0.76 *(5.75)*	1.84 *(68.99)*	2.00 *(100.00)*	1.88 *(75.15)*	2.28 *(190.55)*
97 LE	0.36 *(2.29)*		0.39 *(2.45)*		1.58 *(37.61)*		1.85 *(70.93)*	
181 RE	0.77 *(5.84)*	0.78 *(6.03)*	0.61 *(4.08)*	0.84 *(6.92)*	**2.00 *(99.12)***	2.00 *(100.00)*	2.17 *(147.66)*	2.37 *(234.42)*
181 LE	**1.23 *(16.83)***		**1.30 *(20.09)***		**2.00 *(99.01)***		**2.47 *(293.25)***	
273 RE	0.45 *(2.80)*	0.74 *(5.50)*	0.57 *(3.70)*	0.81 *(6.46)*	1.98 *(96.30)*	2.00 *(100.00)*	2.13 *(134.70)*	2.33 *(213.80)*
273 LE	0.39 *(2.43)*		0.63 *(4.22)*		1.93 *(84.40)*		1.93 *(85.52)*	
361 RE	0.61 *(4.10)*	0.75 *(5.62)*	0.68 *(4.82)*	0.82 *(6.61)*	1.99 *(98.49)*	2.00 *(100.00)*	**2.34 *(217.22)***	2.34 *(218.78)*
361 LE	0.54 *(3.48)*		0.65 *(4.47)*		1.99 *(98.65)*		2.17 *(146.94)*	
Best Vitelliform Macular Dystrophy								
2 RE	**0.73 *(5.33)***	0.53 *(3.39)*	**0.71 *(5.15)***	0.61 *(4.07)*	**2.00 *(99.40)***	2.00 *(100.00)*	**2.23 *(170.40)***	2.14 *(138.04)*
2 LE	**0.88 *(7.54)***		**1.01 *(10.14)***		**2.00 *(99.45)***		**2.55 *(352.10)***	
Central Serous Retinopathy History left eye								
127 RE	0.35 *(2.25)*	0.54 *(3.47)*	0.40 *(2.54)*	0.63 *(4.27)*	1.58 *(38.34)*	2.00 *(100.00)*	1.88 *(76.58)*	2.15 *(141.25)*
127 LE	0.31 *(2.05)*		0.45 *(2.83)*		1.88 *(75.59)*		1.81 *(64.83)*	
Macular Pucker left eye								
211 RE	0.52 *(3.31)*	0.73 *(5.37)*	0.42 *(2.66)*	0.80 *(6.31)*	1.79 *(62.08)*	2.00 *(100.00)*	2.07 *(116.53)*	2.32 *(208.93)*
211 LE	0.54 *(3.44)*		0.62 *(4.21)*		1.93 *(85.28)*			

Table 7.8 (Continued)

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Ablatio Retinae history both eyes								
291 RE	0.35 *(2.26)*	0.66 *(4.57)*	0.46 *(2.88)*	0.74 *(5.50)*	1.80 *(62.99)*	2.00 *(100.00)*	2.01 *(101.90)*	2.25 *(177.83)*
291 LE	0.59 *(3.89)*		0.52 *(3.33)*		1.95 *(89.46)*		**2.28 *(188.84)***	
Ablatio Retinae history right eye								
266 RE	-	0.63 *(4.27)*	-	0.71 *(5.13)*	-	2.00 *(100.00)*	-	2.22 *(165.96)*
266 LE	0.61 *(4.04)*		0.65 *(4.44)*		1.96 *(91.76)*		2.17 *(148.63)*	
Macular Star (Exudates) left eye								
129 RE	**0.72 *(5.19)***	0.72 *(5.25)*	0.66 *(4.62)*	0.79 *(6.17)*	**2.00 *(99.54)***	2.00 *(100.00)*	2.20 *(156.74)*	2.31 *(204.17)*
129 LE	**1.06 *(11.45)***		**1.07 *(11.73)***		**2.00 *(99.52)***		**2.60 *(400.89)***	
Roth Spot left eye								
88 RE	**0.73 *(5.35)***	0.56 *(3.63)*	0.52 *(3.32)*	0.65 *(4.47)*	**2.00 *(99.13)***	2.00 *(100.00)*	**2.41 *(259.46)***	2.17 *(147.91)*
88 LE	0.42 *(2.61)*		0.58 *(3.79)*		1.97 *(93.06)*		1.97 *(93.43)*	

Table 7.8 Mesopic VA thresholds in logMAR and mesopic FCS thresholds in log (% contrast) of participants with fundus abnormalities. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.8. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

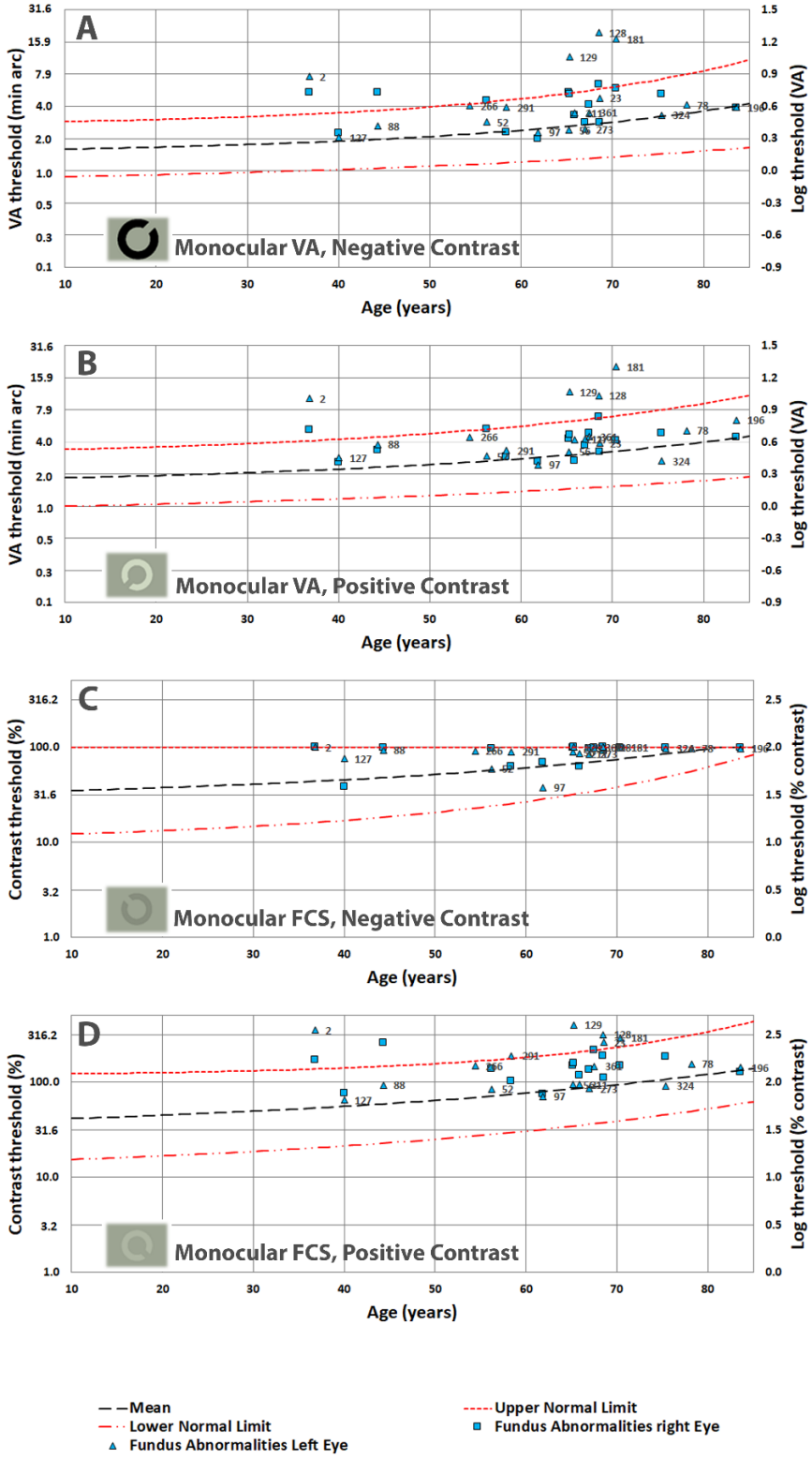


Figure 7.8 (A-D) Mesopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with fundus abnormalities plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of mesopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.9.2 Amblyopia

Table 7.9 lists the mesopic results of the participants with amblyopia with the calculated corresponding upper normal limits for each individual. In this table, individuals are categorized as amblyopia right eye and amblyopia left eye. The mesopic VA and FCS results are comparable with the photopic results. Most of the amblyopic eyes do have thresholds above the upper normal limits, with only a few exceptions. The amblyopic and contralateral eye thresholds are plotted in figure 7.9 (A-D). This figure illustrates how the thresholds are related to the means, upper normal limits and lower normal limits based on participants with normal visual performance.

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Amblyopia: Amblyopia right eye								
39 RE	**0.64** ***(4.34)***	0.46 *(2.88)*	**0.69** ***(4.85)***	0.54 *(3.47)*	**2.00** ***(99.15)***	2.00 *(100.00)*	**2.32** ***(210.62)***	2.09 *(123.03)*
39 LE	0.36 *(2.27)*		**0.55** ***(3.52)***		1.96 *(90.96)*		2.01 *(103.04)*	
169 RE	0.42 *(2.63)*	0.62 *(4.17)*	0.42 *(2.61)*	0.70 *(5.01)*	1.95 *(88.93)*	2.00 *(100.00)*	1.90 *(79.02)*	2.21 *(162.18)*
169 LE	0.31 *(2.02)*		0.29 *(1.95)*		1.62 *(41.62)*		1.79 *(61.61)*	
264 RE	**0.58** ***(3.77)***	0.55 *(3.55)*	**0.67** ***(4.69)***	0.64 *(4.37)*	**1.99** ***(98.26)***	2.00 *(100.00)*	**2.27** ***(188.17)***	2.16 *(144.54)*
264 LE	0.52 *(3.33)*		0.56 *(3.66)*		1.89 *(77.07)*		2.06 *(114.98)*	
300 RE	-	0.60 *(3.98)*	-	0.68 *(4.79)*	-	2.00 *(100.00)*	-	2.20 *(158.49)*
300 LE	0.28 *(1.92)*		0.32 *(2.08)*		1.63 *(42.86)*		1.65 *(44.40)*	
309 RE	**0.62** ***(4.15)***	0.47 *(2.95)*	**0.60** ***(4.02)***	0.55 *(3.55)*	**1.98** ***(95.75)***	2.00 *(100.00)*	**2.23** ***(167.98)***	2.10 *(125.89)*
309 LE	0.43 *(2.67)*		0.50 *(3.18)*		1.84 *(69.38)*		1.96 *(90.56)*	
Amblyopia left eye								
70 RE	0.42 *(2.64)*	0.64 *(4.37)*	0.47 *(2.92)*	0.72 *(5.25)*	1.84 *(69.17)*	2.00 *(100.00)*	1.92 *(83.81)*	2.24 *(173.78)*
70 LE	**0.74** ***(5.55)***		**0.86** ***(7.22)***		1.99 *(98.46)*		**2.51** ***(323.94)***	
138 RE	0.27 *(1.87)*	0.48 *(3.02)*	0.33 *(2.15)*	0.56 *(3.63)*	1.70 *(49.91)*	2.00 *(100.00)*	1.79 *(61.47)*	2.10 *(125.89)*
138 LE	0.43 *(2.70)*		0.30 *(1.98)*		1.72 *(52.87)*		1.98 *(94.48)*	
199 RE	0.42 *(2.66)*	0.59 *(3.89)*	0.41 *(2.60)*	0.68 *(4.79)*	1.83 *(68.08)*	2.00 *(100.00)*	1.94 *(86.40)*	2.19 *(154.88)*
199 LE	**0.68** ***(4.79)***		**0.72** ***(5.29)***		**2.00** ***(99.45)***		2.11 *(129.96)*	
201 RE	0.53 *(3.38)*	0.92 *(8.32)*	0.56 *(3.65)*	0.95 *(8.91)*	1.98 *(95.79)*	2.00 *(100.00)*	1.29 *(89.04)*	2.52 *(331.13)*
201 LE	-		-		-		-	
238 RE	0.66 *(4.57)*	0.68 *(4.79)*	0.69 *(4.86)*	0.75 *(5.62)*	1.99 *(98.82)*	2.00 *(100.00)*	2.26 *(183.72)*	2.27 *(186.21)*
238 LE	-		-		-		-	
272 RE	0.22 *(1.65)*	0.51 *(3.24)*	0.30 *(1.99)*	0.59 *(3.89)*	1.58 *(37.72)*	2.00 *(100.00)*	1.67 *(46.54)*	2.13 *(134.90)*
272 LE	**0.64** ***(4.34)***		**0.67** ***(4.66)***		1.99 *(98.78)*		1.93 *(85.32)*	
276 RE	0.45 *(2.81)*	0.65 *(4.47)*	0.51 *(3.23)*	0.73 *(5.37)*	1.98 *(96.47)*	2.00 *(100.00)*	2.06 *(115.36)*	2.25 *(177.83)*
276 LE	0.50 *(3.19)*		0.51 *(3.26)*		1.93 *(85.53)*		1.93 *(85.05)*	
287 RE	0.42 *(2.65)*	0.60 *(3.98)*	0.46 *(2.87)*	0.68 *(4.79)*	1.87 *(73.78)*	2.00 *(100.00)*	1.90 *(79.60)*	2.20 *(158.49)*
287 LE	**0.72** ***(5.21)***		**0.82** ***(6.63)***		**2.00** ***(99.54)***		**2.56** ***(395.73)***	
313 RE	0.60 *(3.95)*	0.72 *(5.25)*	0.51 *(3.21)*	0.79 *(6.17)*	1.98 *(96.59)*	2.00 *(100.00)*	1.96 *(91.85)*	2.30 *(199.53)*
313 LE	0.44 *(2.77)*		0.54 *(3.48)*		**2.00** ***(99.36)***		2.04 *(110.55)*	
362 RE	0.33 *(2.15)*	0.80 *(6.31)*	0.28 *(1.92)*	0.85 *(7.08)*	1.72 *(52.78)*	2.00 *(100.00)*	1.80 *(62.67)*	2.38 *(239.88)*
362 LE	0.53 *(3.36)*		0.60 *(4.00)*		1.99 *(96.65)*		2.01 *(103.27)*	

Table 7.9 Mesopic VA thresholds in logMAR and mesopic FCS thresholds in log (% contrast) of participants with amblyopia. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.9. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

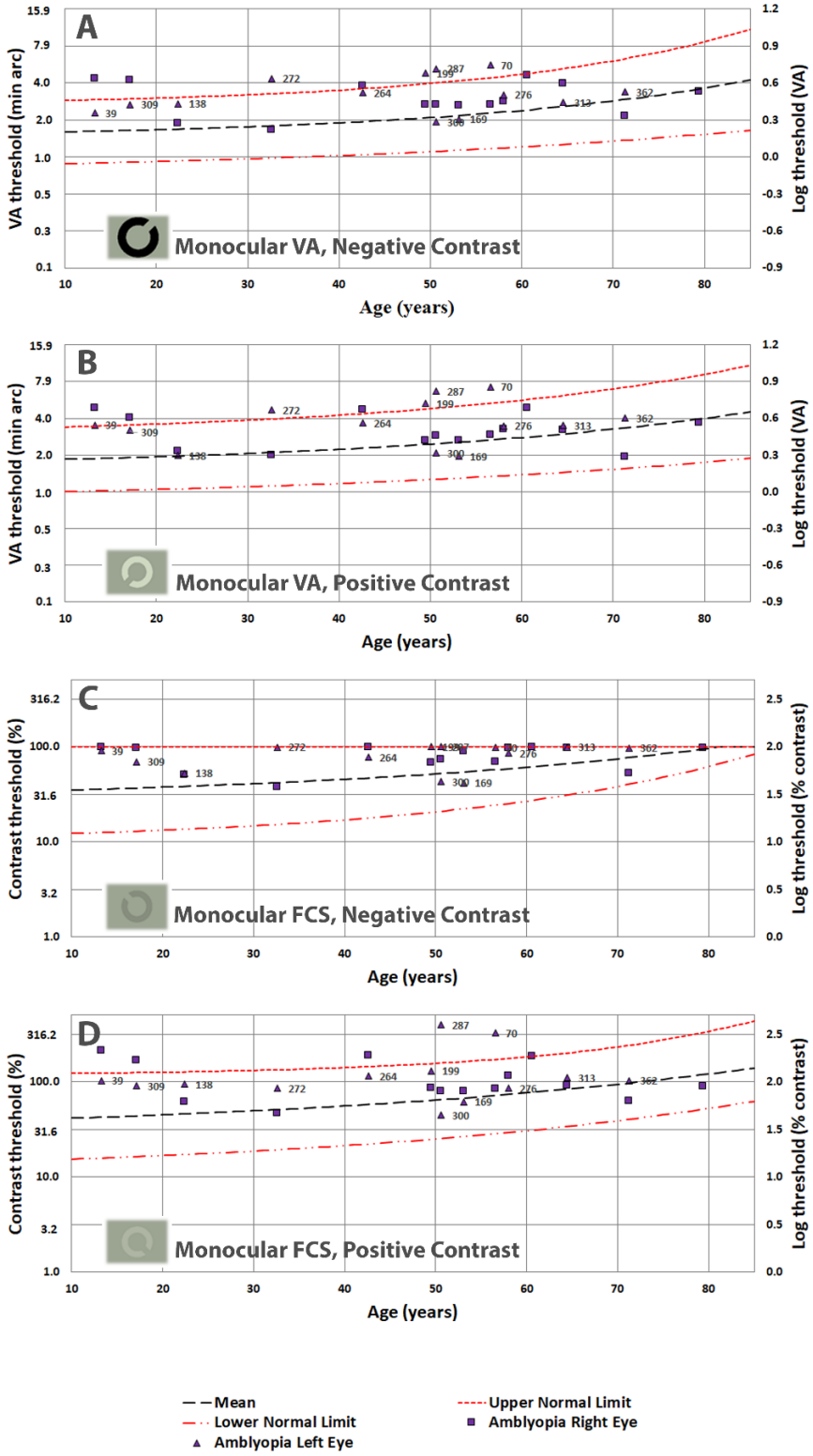


Figure 7.9 (A-D) Mesopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with amblyopia plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of mesopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.9.3 Anterior segment conditions

The Acuity-*Plus* test revealed mesopic VA thresholds outside the normal limits for both contrast polarities in the left eye of participant 51, who underwent refractive laser surgery by LASEK. The other abnormal threshold was found in participant 305, with a history of LASIK refractive surgery laser. The negative contrast VA threshold was outside the normal limits for the right eye positive contrast VA, as were the left eye positive contrast FCS and negative contrast VA in both eyes. The other participant revealed abnormal right eye thresholds for negative and positive contrast VA. One of the two participants with orthokeratology showed a borderline negative contrast VA threshold under mesopic conditions. In one of the two individuals with congenital lens opacities, right and left eye thresholds for mesopic negative contrast VA were outside the normal upper limits. In this participant, visual performance under photopic conditions was better. The same conclusion could be drawn for the participant with keratoconus. The more advanced keratoconus in the right eye resulted in thresholds outside the normal upper limits or borderline for all mesopic measurements. The participants' mesopic VA and FCS thresholds within the anterior segment conditions group are shown in table 7.10 and plotted with the established means, upper normal limits, and lower normal limits in figure 7.10 (A-D).

Participant	Mesopic VA Negative Contrast in logMAR *(MOA)*	Mesopic VA Negative Contrast UNL in logMAR *(MOA)*	Mesopic VA Positive Contrast in logMAR *(MOA)*	Mesopic VA Positive Contrast UNL in logMAR *(MOA)*	Mesopic FCS Negative Contrast in log (%) *(PCT)*	Mesopic FCS Negative Contrast UNL in log (%) *(PCT)*	Mesopic FCS Positive Contrast in log (%) *(PCT)*	Mesopic FCS Positive Contrast UNL in log (%) *(PCT)*
Refractive Laser Surgery								
51 RE	0.24 *(1.73)*	0.55 *(3.55)*	0.40 *(2.51)*	0.63 *(4.27)*	1.68 *(47.54)*	2.00 *(100.00)*	1.92 *(84.05)*	2.15 *(141.25)*
51 LE	**0.71 *(5.16)***		**0.66 *(4.58)***		1.99 *(98.19)*		2.07 *(117.51)*	
156 RE	0.12 *(1.33)*	0.56 *(3.63)*	0.33 *(2.12)*	0.65 *(4.47)*	1.38 *(24.08)*	2.00 *(100.00)*	1.71 *(51.23)*	2.17 *(147.91)*
156 LE	0.16 *(1.44)*		0.19 *(1.56)*		1.35 *(22.30)*		1.54 *(34.29)*	
242 RE	0.30 *(1.98)*	0.54 *(3.47)*	0.27 *(1.85)*	0.62 *(4.17)*	1.77 *(58.41)*	2.00 *(100.00)*	1.88 *(76.50)*	2.15 *(141.25)*
242 LE	0.24 *(1.75)*		0.31 *(2.06)*		1.60 *(39.54)*		1.56 *(36.35)*	
274 RE	0.58 *(3.80)*	0.61 *(4.07)*	0.64 *(4.40)*	0.69 *(4.90)*	1.99 *(96.70)*	2.00 *(100.00)*	1.98 *(95.00)*	2.20 *(158.49)*
274 LE	0.56 *(3.61)*		0.56 *(3.67)*		1.93 *(85.10)*		2.14 *(138.71)*	
281 RE	0.36 *(2.30)*	0.59 *(3.89)*	0.50 *(3.13)*	0.67 *(4.68)*	1.92 *(83.45)*	2.00 *(100.00)*	2.03 *(106.77)*	2.19 *(154.88)*
281 LE	0.41 *(2.58)*		0.47 *(2.92)*		1.89 *(77.88)*		1.88 *(76.07)*	
284 RE	0.31 *(2.02)*	0.60 *(3.98)*	0.36 *(2.28)*	0.68 *(4.79)*	1.81 *(64.32)*	2.00 *(100.00)*	1.87 *(74.36)*	2.20 *(158.49)*
284 LE	0.30 *(2.00)*		0.43 *(2.68)*		1.69 *(49.02)*		1.67 *(46.98)*	
302 RE	0.34 *(2.17)*	0.60 *(3.98)*	0.37 *(2.37)*	0.68 *(4.79)*	1.88 *(75.74)*	2.00 *(100.00)*	1.87 *(74.63)*	2.20 *(158.49)*
302 LE	0.24 *(1.74)*		0.45 *(2.83)*		1.68 *(47.83)*		1.76 *(56.94)*	
305 RE	0.53 *(3.38)*	0.55 *(3.55)*	0.59 *(3.85)*	0.64 *(4.37)*	1.95 *(88.45)*	2.00 *(100.00)*	1.95 *(88.52)*	2.16 *(144.54)*
305 LE	0.47 *(2.95)*		0.50 *(3.18)*		1.90 *(78.94)*		1.96 *(92.13)*	
306 RE	0.28 *(1.89)*	0.55 *(3.55)*	0.36 *(2.31)*	0.64 *(4.37)*	1.58 *(38.31)*	2.00 *(100.00)*	1.78 *(60.49)*	2.16 *(144.54)*
306 LE	0.27 *(1.86)*		0.41 *(2.55)*		1.56 *(36.17)*		1.75 *(56.39)*	
382 RE	0.20 *(1.58)*	0.49 *(3.09)*	0.15 *(1.40)*	0.56 *(3.63)*	1.37 *(23.22)*	2.00 *(100.00)*	1.45 *(28.22)*	2.11 *(128.82)*
382 LE	0.18 *(1.50)*		0.27 *(1.87)*		1.41 *(25.44)*		1.42 *(26.39)*	
Orthokeratology								
155 RE	**0.47 *(2.92)***	0.47 *(2.95)*	0.44 *(2.77)*	0.54 *(3.47)*	1.89 *(77.96)*	2.00 *(100.00)*	1.85 *(71.26)*	2.09 *(123.03)*
155 LE	0.20 *(1.60)*		0.26 *(1.84)*		1.58 *(37.73)*		1.58 *(37.73)*	
212 RE	0.47 *(2.97)*	0.53 *(3.39)*	0.57 *(3.72)*	0.62 *(4.17)*	1.93 *(84.72)*	2.00 *(100.00)*	2.04 *(109.79)*	2.14 *(138.04)*
212 LE	0.35 *(2.25)*		0.52 *(3.30)*		1.87 *(74.82)*		1.87 *(74.82)*	
Congenital Lens Opacities								
19 RE	**0.49 *(3.06)***	0.47 *(2.95)*	0.37 *(2.33)*	0.54 *(3.47)*	1.79 *(60.97)*	2.00 *(100.00)*	1.86 *(72.62)*	2.09 *(123.03)*
19 LE	**0.51 *(3.23)***		0.47 *(2.97)*		1.88 *(76.37)*		1.90 *(79.64)*	
192 RE	0.19 *(1.54)*	0.48 *(3.02)*	0.18 *(1.53)*	0.56 *(3.63)*	1.46 *(29.09)*	2.00 *(100.00)*	1.25 *(17.98)*	2.10 *(125.89)*
192 LE	0.34 *(2.19)*		0.43 *(2.70)*		1.65 *(44.84)*		1.84 *(68.60)*	
Keratoconus								
214 RE	**0.70 *(5.06)***	0.57 *(3.72)*	**0.77 (5.83)**	0.65 *(4.47)*	**2.00 *(100.00)***	2.00 *(100.00)*	**2.39 *(242.75)***	2.17 *(147.91)*
214 LE	0.39 *(2.45)*		0.36 *(2.31)*		1.78 *(60.75)*		1.94 *(87.28)*	

Table 7.10 Mesopic VA thresholds in logMAR and mesopic FCS thresholds in log (% contrast) of participants with anterior segment conditions. The corresponding VA in minutes of arc and FCS in percentage are also given. Upper normal limits corresponding with the age of the participant for each measurement are listed in the table. Thresholds outside normal limits are presented in bold. Participant numbers correspond with the numbers in figure 7.10. Abbreviations: logMAR = logarithm of the minimum angle of resolution; MOA = minutes of arc; log = logarithm; PCT = percentage; VA = visual acuity; FCS = functional contrast sensitivity; RE = right eye; LE = left eye; UNL = upper normal limit.

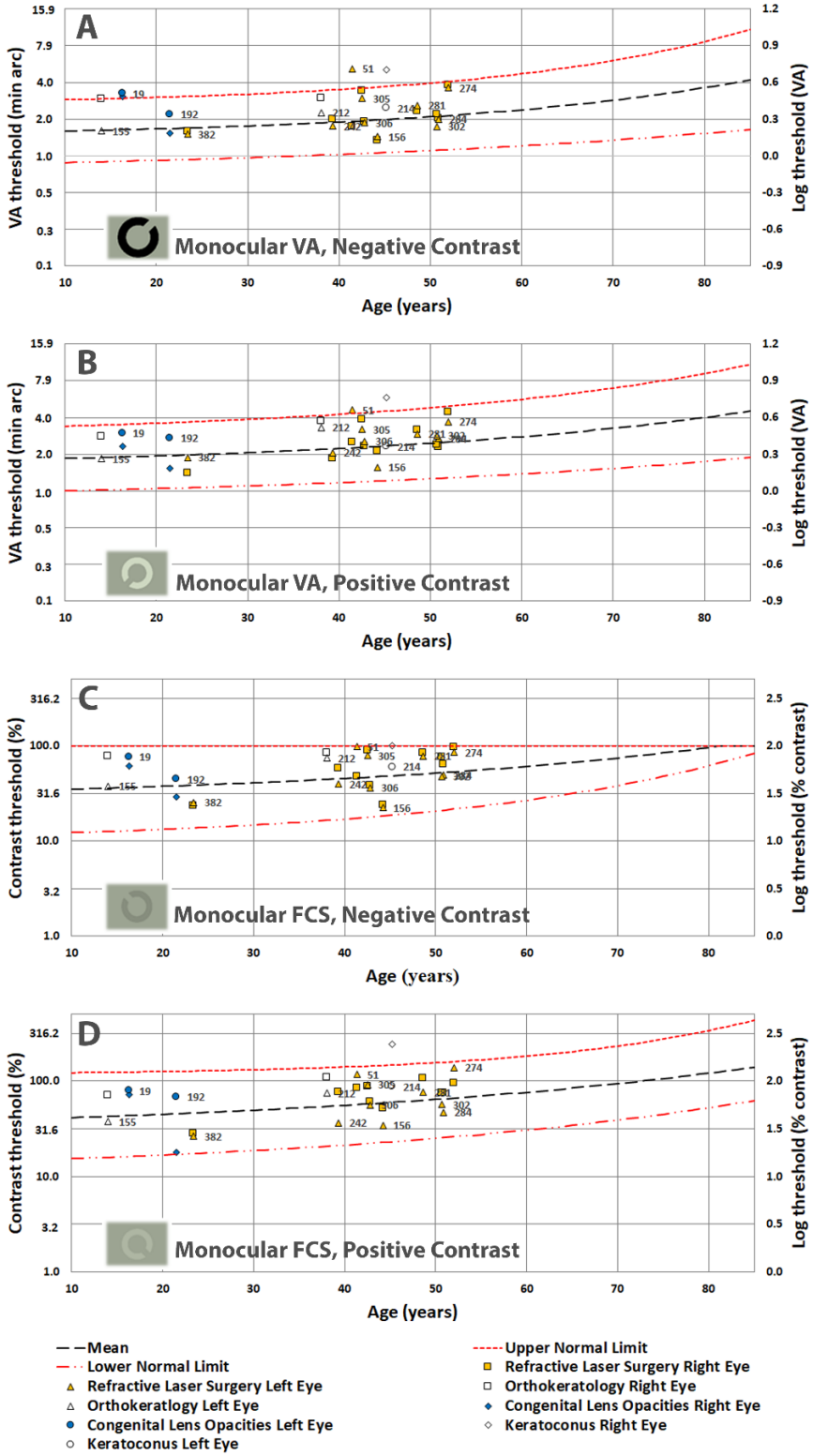


Figure 7.10 (A-D) Mesopic monocular (right and left eye data) VA thresholds in logMAR units and the corresponding minutes of arc, and FCS thresholds in log units and the corresponding percentage luminance contrast of participants with anterior segment conditions plotted with the means, upper normal limits and lower normal limits based on the results of the participants with normal visual performance. The graphs show the results of mesopic monocular negative contrast VA (A), monocular positive contrast VA (B), monocular negative contrast FCS (C) and monocular positive contrast FCS (D).

7.9.4 Lens Opacities

The effect of lens opacities on mesopic spatial vision was also analysed in the participants who fulfilled the criteria for normal mesopic visual performance. This was limited to the lower grades (0, 1 and 2) according to the Optometry Grading Scale, as grades 3, 4 and 5 were excluded. Similar to photopic conditions, analyses were only performed for the effect of nuclear opacities. The number of participants with cortical and posterior subcapsular cataracts was insufficient to obtain reliable results. Independent t-tests were performed in the mesopic right and left eye separately, and the right or left eye randomised for negative contrast VA, positive contrast VA, negative contrast FCS and positive contrast FCS results. Comparisons between nuclear lens gradings of 0 and 1 were conducted for the second and third decade, and between 1 and 2 for the fourth, fifth and sixth decade. Thresholds were slightly increased with higher grading of lens opacities. Despite that, with one exception, all the comparisons were not statistically different ($P>0.006$). The only statistically significant difference was found in the sixth decade between nuclear cataract grades 1 and 2 with mesopic negative contrast VA for the left eye ($P<0.006$).

7.10 Discussion

A highly exploratory study was conducted to evaluate the application of established normal limits in participants suffering from any systemic or ocular condition. With respect to vascular conditions, participants with hypertension without retinopathy were analysed and considered to be normal as hypertension is common in the general population (Blokstra et al., 2011; Nielen et al., 2020; Klijs et al., 2015). No statistical differences in VA and FCS thresholds were found between participants with hypertension and age-matched controls in both light conditions and contrast polarities. The remaining systemic diseases were excluded if the number of participants was too low for reliable statistical analysis. The results from the participants with diabetes suggest that spatial vision could be affected, even in the absence of diabetic retinopathy. Mesopic VA and FCS thresholds were more affected than photopic. These findings are in agreement with other previous studies (O'Neill-Biba et al., 2010; Katz et al., 2010; Pramanik et al., 2020). It has been shown that the effect of diabetes is not limited to the microvasculature, but the neurovascular unit of the retina is also involved (Gardner and Davila, 2017). The effect of diabetes on the neuroretina cannot be established with fundoscopy but requires visual function tests such as CS to establish any effect (Joltikov et al.,

2018; Jackson et al., 2012; Joltikov et al., 2017). These functions can be impaired without signs of diabetic retinopathy and in the presence of good photopic VA. Some participants in the group with hyperlipidemia showed VA and FCS thresholds outside normal limits in both light conditions. In clinical practice it would be recommended to invite the patient for follow up measurements to monitor for changes. Previous studies have found an effect of high-density lipoprotein (HDL) cholesterol on contrast thresholds and CSF particularly in patients with diabetes (Olmedilla-Alonso et al., 2021). CS was more affected in patients with diabetes in combination with hyperlipidemia (Olmedilla-Alonso et al., 2021).

Results from one of the four participants with rheumatoid arthritis showed affected mesopic VA and FCS in positive contrast for one eye; the other eye showed normal visual performance. All photopic measurements were within normal limits. It is well known that rheumatoid arthritis can cause dry eyes, and the severity correlates with the disease's duration (Abd-Allah et al., 2020). Dry eyes are associated with a decrease of VA and CS (Szczotka-Flynn et al., 2019). However, none of the rheumatoid arthritis participants in our study had complaints or signs of dry eyes. Furthermore, the effect of rheumatoid arthritis medications can also affect CS (Singla et al., 2021). The participant with the abnormal mesopic thresholds was using Hydroxychloroquine, which can affect spatial vision (Singla et al., 2021). CS measurements should be considered when screening for Hydroxychloroquine toxicity, and a decrease may be an early sign of visual dysfunction (Singla et al., 2021).

Allergic rhinitis can cause several ocular symptoms, such as itching, watering, redness and swollen eyelids. These symptoms can affect visual performance, and the severity often depends on the season (Klossek et al., 2012). None of the participants with allergic rhinitis showed VA and FCS thresholds outside the normal limits in both light conditions. Despite participants performed the tests during hay fever season, no abnormalities were found with the eye examinations.

It is well known that thyroid disorders may affect tear film stability (Alanazi et al., 2019), resulting in a decrease of VA and CS (Szczotka-Flynn et al., 2019). However, the participants with a thyroid disorder included in this study showed normal photopic and mesopic VA and FCS thresholds.

The participant with multiple sclerosis showed normal VA and FCS thresholds for their age in photopic and mesopic conditions. There was no history of optic neuritis, which can affect VA and FCS (Trobe et al., 1996). The decrease in CS may be present in both eyes, even if optic neuritis seems unilateral (Nordmann, Saraux and Roullet, 1987). In the current study, OCT imaging was not carried out in most

participants. This would have been of value if macular, retinal nerve fiber layer and ganglion cell layer thinning observed with OCT imaging could be correlated with decreases of VA and CS in multiple sclerosis patients (Satue et al., 2016).
One of the two participants with epilepsy had thresholds outside the normal limits in both light conditions in one eye. Both participants were using the medication Lamotrigne, which may have ocular side effects such as blurred vision (Hilton, Hosking and Betts, 2004) and may account for the findings.
Both participants with ADHD had abnormal VA and FCS thresholds for one or more measurements, which agrees with previous studies (Kim, Chen and Tannock, 2014). It has been demonstrated that individuals with ADHD reported more problems in daily life tasks such as depth perception, peripheral vision, visual search and visual processing speed (Kim, Chen and Tannock, 2014). CS was previously suggested as a physiological biomarker in ADHD (Bubl et al., 2013; Dönmez et al., 2020).
It is known that ocular conditions can affect VA and CS, particularly under mesopic conditions (Petzold and Plant, 2006). The effect of AMD on spatial vision is often reported, and both VA and CS are often decreased in patients with AMD (Puell et al., 2012; Kleiner et al., 1988). The decrease of mesopic spatial vision is more pronounced than under photopic conditions (Puell et al., 2012). These findings are in agreement with the results of the participants with AMD enrolled in this study. In both light conditions, several participants with AMD showed VA and FCS thresholds outside the normal limits. The participants were categorized as having either hyper- and hypopigmentation or macular degeneration. This classification was chosen as it was unclear whether the hypo- and hyperpigmentation were an early sign of AMD, or had a different origin. The participants with macular degeneration also showed drusen or geographic areas in the macula. The decrease of VA and FCS thresholds were more severe in mesopic conditions, and one of the participants with AMD was unable to perform the test in mesopic conditions for the most affected eye. Two participants with hypo- and hyperpigmentation of the macula showed suspicious VA and FCS thresholds, particularly under mesopic conditions. In both participants photopic high contrast acuity with the ETDRS chart were within normal limits. One did not have any visual complaints, and the other reported complaints in reduced light conditions. A follow-up within three years revealed progression to AMD in both cases, and one was not able to carry out the Acuity-*Plus* test again due to geographic atrophy. These findings showed the importance of the different monocular test conditions in clinical practice. Participants with suspicious thresholds can be advised to get an exam at least once a year to keep track on any changes.
These results are also in accordance with the previous finding that decreased

mesopic acuity can precede developing AMD within three years in participants with normal macular health (Owsley et al., 2016a).

The results from the participant with Best's vitelliform macular dystrophy stage three (pseudo hypopyon), which can also affect the macular area, was similar to participants suffering from age-related macular degeneration. Most of the VA and FCS thresholds were outside normal photopic and mesopic conditions limits. However, the mesopic VA and FCS were more affected than the photopic thresholds.

All the photopic and mesopic measurements of the participant with a history of resolved central serous retinopathy were inside normal limits. It has previously been established that VA can recover to normal after central serous retinopathy; however, CS does not necessarily recover in all patients (Maaranen and Mäntyjärvi, 1999; Baran, Gürlü and Esgin, 2005). More participants need to be included to perform reliable statistical analysis to investigate the differences between VA and FCS recovery after central serous retinopathy in photopic and mesopic conditions.

The inner retinal function in patients with a macular pucker may be altered. Previous findings showed that these changes might result in reduced CS (Nguyen et al., 2014). In contrast, the participant with a macular pucker in this exploratory study, revealed normal VA and FCS thresholds in photopic and mesopic conditions.

The participant with a history of ablatio retinae in both eyes had FCS thresholds outside normal limits for one eye in mesopic positive contrast. The other participant with a history of ablatio retinae in one eye, was unable to perform the test in the affected eye.

The effect of a previous retinal detachment on spatial vision is dependent on macular involvement (Anderson and Sjöstrand, 1981; Ross, 2002). The information about the type of detachments (macular on or off) in this study were unavailable.

Glaucoma is known to affect peripheral vision, causing visual field defects. In visual field assessment, a central decrease in sensitivity requires more ganglion cell loss due to the higher density of these cells in the fovea (Kim and Mayer, 1994). Previous studies have found that the macular ganglion cell inner plexiform layer thickness can discriminate between healthy and glaucomatous eyes and between consecutive glaucoma stages (Ustaoglu, Solmaz and Onder, 2019). Despite good VA, it has also been shown that photopic and mesopic CS is impaired in glaucoma patients (Lahav et al., 2011). As a result of the higher density of ganglion cells in the central retina, CS may be more sensitive in comparison with high contrast acuity (Lahav et al., 2011). In this study, a substantial percentage of glaucoma participants had FCS thresholds outside or close to the upper normal limit. However, in some

glaucoma participants, VA was also affected, and it seems that the effect was more pronounced under mesopic conditions. Further investigation is needed to determine the sensitivity of the Acuity-*Plus* test in detection and screening of the progression of glaucoma.

As expected, most amblyopic eyes showed VA and FCS thresholds outside normal limits in both light conditions. These findings are in agreement with other studies (Lew et al., 2003; Webber and Wood, 2005). It is well known that VA and CS are correlated (Moseley et al., 2006); however, VA cannot predict CS (Haegerstrom-Portnoy et al., 2000). Despite the fact that VA can recover to normal age-related values with treatment, CS may not show the same progress (Wang et al., 2017). Performance of CS will be lower in amblyopic patients, particularly in low illuminance levels (Wang et al., 2017). It would be of interest to measure FCS in amblyopia treatment for photopic and mesopic light conditions. The established age-related normal values of spatial vision in photopic and mesopic light conditions would be beneficial in such treatments.

The VA and FCS thresholds of participants who underwent refractive laser surgery, indicated that spatial vision might be affected. Previous studies have shown that refractive laser surgery can affect CS (Lee et al., 2006; Montés-Micó, España and Menezo, 2003). It has been reported that the deterioration of CS and increased glare, halo's and starburst effects result from higher-order aberration induced by refractive laser surgery (Wang et al., 2018; Keir et al., 2009). However, the results in this study were not consistent, some participants showed excellent spatial vision after refractive laser surgery while others had reduced functions. Gao et al. (2021) found no significant differences between preoperative and three months postoperative photopic and mesopic CS thresholds (Gao et al., 2021). There was no opportunity to compare preoperative and postoperative results in this study, which is crucial to evaluate if the treatment contributes to the decrease of spatial vision. Additionally, sample sizes were too small to evaluate the effect of each type of surgery. Furthermore, the laser surgery treatments were only subdivided by the procedures. More specific information about the treatment is essential, for example, if the treatment was wavefront-guided and/or a microkeratome or femtosecond laser was used in LASIK. Wavefront guided LASIK, and using a femtosecond laser instead of a microkeratome, results in a reduction of higher-order aberrations and better CS (Zhang et al., 2013; Xia et al., 2015).

Higher-order aberrations increases are also reported in overnight orthokeratology wearers and related to a decrease in CS (Hiraoka et al., 2007; Hiraoka et al., 2008; Chang and Cheng, 2020). A small treatment zone and decentration of the lens may

also contribute to CS deterioration (Liu et al., 2018). In one of the two orthokeratology wearers negative contrast VA of the right eye showed a borderline threshold. This could be due to the increase of the pupil size in mesopic conditions, which is related with an increase of higher-order aberrations (Wang et al., 2003). Evidence suggests that keratoconus affects spatial vision, in both photopic and mesopic conditions (Asgari et al., 2018; Carballo et al., 2013). The severity of the keratoconus is correlated with a decrease in VA and CS (Liduma, Luguzis and Krumina, 2020). The correlation is more pronounced in CS compared with VA (Liduma, Luguzis and Krumina, 2020). Despite good VA, CS may be reduced compared to healthy age-matched controls (Shneor, Piñero and Doron, 2021). The main reason for the decrease in spatial vision in patients with keratoconus is also the increase in higher-order aberrations (Shneor, Piñero and Doron, 2021). The keratoconus participant who completed the Acuity-*Plus* test in this study showed thresholds in agreement with the results of previous studies (Shneor, Piñero and Doron, 2021). The eye with more advanced keratoconus showed abnormal performance in photopic positive contrast FCS. In mesopic conditions all VA and FCS performance were outside the normal limit or borderline.

Differences between nuclear cataract gradings following the Optometry Grading Scale were analysed in this study per decade. Overall, VA and FCS thresholds were slightly higher in photopic and mesopic conditions with an increase of cataract grading. However, the difference was only statistically significant between grade one and two in the sixth decade with mesopic negative contrast FCS (P<0.006). In this study the number of participants with cortical and posterior subcapsular cataracts was too low for reliable analysis. Previous studies have investigated the effect of these two cataract types on spatial vision, and the effect is more pronounced than in nuclear cataracts (Lasa et al., 1993). In addition, it has been demonstrated that low grade nuclear cataract has more negligible effect on VA and CS (Elliott, D. B., Gilchrist and Whitaker, 1989; Shandiz et al., 2011). Interocular scatter and higher-order aberrations contribute to the decrease in VA and CS in cataracts (Shandiz et al., 2011). The deterioration in spatial vision is more evident in mesopic conditions compared with photopic conditions (Weiss, 1990; Hertenstein et al., 2016). One of the two participants with congenital lens opacities showed abnormal mesopic negative contrast VA thresholds in both eyes. In photopic conditions positive contrast VA of the left eye was outside the normal limit. The other participant had normal thresholds for all measurements. The effect of location and density of the lens opacities on VA and FCS needs to be further investigated.

7.11 Conclusions

This highly exploratory study showed that the established age-related normal limits are useful in screening for systemic and ocular conditions in clinical practice. In addition, the normal limits can be applied in the investigation of the effect of specific ocular conditions on photopic and mesopic VA and FCS thresholds. The standardized protocol in both light conditions, allows comparisons of the results of different ocular conditions. The number of participants within the different conditions was too low to determine the effect of the different diseases on spatial vision. More investigation is needed to establish the effect of the different diseases on photopic and mesopic VA and FCS using the standard protocol of the Acuity-*Plus* test in negative and positive contrast.

7.12 Recommendations future work

It would be of interest to investigate the effect of different systemic diseases on photopic and mesopic Acuity-*Plus* VA and FCS thresholds with adequate numbers of participants. Including a complete health examination and disease classified by severity gradings and control of the condition would be beneficial. Blood tests, use of medications and disease control status should be part of such a study. In such a study, it is also important to consider the possible effects of medications as these can affect spatial vision. This is idealistic, in older people the results to define the effect of one condition can be affected by many factors, such as comorbidities and multiple medications. A compromise could be to include a medical examination and blood tests of the most common diseases that can affect the eye, such as diabetes. To investigate the effect of ocular disease on VA and FCS thresholds obtained with the Acuity-*Plus* test accurately, more participants for each condition need to be included. Furthermore, it is of importance to classify the participants following the grading systems of the disease, for example the gradings for AMD. It would also be of interest to investigate the effect of the three types of cataract on VA and FCS thresholds with the Acuity-*Plus* test, with a larger sample size and including more severe gradings. The inclusion of more participants for each systemic and ocular condition will also provide more information about the differences in sensitivity between photopic and mesopic measurements, and between negative and positive contrast optotypes. In addition, the effect of the presentation time in ocular conditions is of interest and should be investigated. In systemic and ocular disease, the brief presentation time may be more sensitive in comparison with continuous viewing spatial vision tests. The effect of amblyopia on spatial vision in photopic and

mesopic conditions has been documented. However, it would be of interest to investigate the effect of the presentation time in amblyopic eyes. Furthermore, to evaluate differences in VA and FCS performance between the different types of amblyopia, it is of importance to include more participants and classify the amblyopia type.

8. Conclusions

The overall aim of this study was to investigate the effect of ageing on spatial vision under both photopic and high mesopic conditions. A novel approach was developed to separate participants who could not be classed as having either normal vision under photopic and mesopic conditions. The same approach may turn out to be also useful in other studies designed to investigate the effects of normal ageing on other aspects of visual performance. VA and FCS thresholds were measured monocularly in each eye and also binocularly with both negative and positive contrast optotypes using a standardized protocol. VA, FCS and the overall variability were found to be age-invariant up to the age of ~50 years in photopic conditions. Under mesopic conditions, an age-invariant limit of ~ 30 years was appropriate. Above 30 years of age, a gradual, but accelerating increase in both variability and mean thresholds were found. Binocular VA and FCS measurements revealed smaller thresholds and less variability compared with the monocular results. Comparisons between the negative and positive contrast optotypes results were conducted, and negative contrast thresholds were significantly better. Normal age-related VA and FCS limits were determined for all sixteen stimulus conditions. VA and FCS thresholds can be measured together in a single test to assess whether an applicant's spatial vision can be classed as normal. The test is simple to carry out and can be implemented in both clinical practice and in occupational settings.

The normal upper threshold limits for spatial vision established in this study for photopic and mesopic conditions were tested out in participants with specific systemic or ocular conditions. The monocular thresholds limits are of greater use in the clinic whilst binocular threshold limits are more applicable for use in visually demanding occupations. The standardized protocols make it possible to compare results in patients with different systemic and ocular conditions. Further investigation is needed to determine the effect of the different conditions on spatial vision in both light conditions and contrast polarities. The numbers of participants in the different clinical groups investigated in this study were too small, and more extensive medical examinations and specific categorization of the conditions are needed. These preliminary findings are of interest since they show how the age-related normal limits established in this study can be applied in screening for abnormal responses and also for the monitoring of disease progression or treatment efficacy in clinical practice.

Appendices

Appendix A: Repeatability of Photopic and Mesopic VA and FCS measurements using the Acuity-*Plus* test

Introduction

Photopic VA measurements are common in clinical practice, for example to establish the best VA with and without prescription, and to detect or monitor the progression of ocular disease. However, it is not always the best predictor of visual performance in daily life, as discussed in chapter 3. Measurements such as mesopic VA, photopic FCS and mesopic FCS are more sensitive to predict visual performance (Wood and Owens, 2005; Maynard, Zele and Feigl, 2016; Müller et al., 2019; Bittner and Ferraz, 2020). However, these measurements are not routine examinations in clinical practice (Wood and Owens, 2005; Maynard, Zele and Feigl, 2016; Müller et al., 2019; Bittner and Ferraz, 2020), mainly because these tests are considered difficult to carry out in a clinical setting. However the introduction of computerized VA and CS tests, generates opportunities to develop accessible and user friendly measurements in photopic and mesopic conditions. There are several tests currently available to establish VA and CS thresholds in clinical practice. However, to interpret VA and CS changes correctly, knowledge about the test's repeatability is important. In previous studies good repeatability was found in photopic high contrast VA testing, for example with the ETDRS and Bailey-Lovie charts (Lovie-Kitchin, 1988; Lovie-Kitchin and Brown, 2000; Reeves, Wood and Hill, 1993; Elliott and Sheridan, 1988; Camparini et al., 2001) and using CS charts for example the Pelli-Robson chart (Elliott, Sanderson and Conkey, 1990; Dougherty, Flom and Bullimore, 2005; Osman et al., 2021). In mesopic conditions the ETDRS VA and Pelli-Robson CS showed also good test-retest repeatability (Barrio, Antona and Puell, 2015).

Test-retest repeatability results depend strongly on the test carried out. For example, the computer-based FRACT test revealed slightly more variation between the two VA measurements than the ETDRS chart (Bach, 2007). Currently, no information exists about the test-retest repeatability of VA and FCS measurements using the Acuity-*Plus* test. Given the test is the mainstay of the results presented in this thesis, we have carried out this study to establish the test-retest repeatability of VA and FCS measurements with the Acuity-*Plus* test in both light conditions and contrast polarities.

Methods

This study was conducted at one testing site; Damme Optometrie, Kesteren and all measurements were carried out by one examiner. A thorough eye examination was carried out as described in section 4.4. All the 25 participants passed the strict definition of normal visual performance in photopic and mesopic light conditions (see section 4.5). All monocular and binocular VA and FCS measurements with the Acuity-*Plus* test were performed twice in both light conditions and contrast polarities. The two measurements were taken on different days to prevent fatigue, but always within one month.

Statistical Analysis

For each monocular and binocular measurement in both light conditions and contrast polarities, Bland-Altman plots were produced (Altman and Bland, 1983). Repeatability was assessed by determining the 95% limits of agreements (LoAs) ± 1.96 standard deviations of the difference between tests. It is of importance to estimate how reliable these LoAs are, in particular with small sample sizes (Bunce, 2009; Carkeet, 2020; Carkeet, 2015). The LoAs in a Bland-Altman estimates what the LoAs might be in a population (Carkeet, 2015). However, the LoAs in specific samples, particularly in small samples, can vary from the limits based on the population (Carkeet, 2015). In this study, the confidence intervals (CIs) of the LoAs were calculated by the exact two-sided tolerance approach. These CIs describe the range in which a measurement is likely to lie for the specific sample with a probability of 95%.

Results

Repeatability measurements were obtained in 25 healthy participants all of whom fulfilled the selection criteria for normal photopic and mesopic conditions. The mean age of participants was 33.8±15.1 years (range 14.1 – 70.3 years), and the group consisted of 15 females and 10 males. All repeatability measurements were performed under the same testing conditions as described in the method section (Section 4.3). The VA and FCS measurements were taken twice for each of the 25 participants, under both photopic and mesopic conditions. The two measurements were performed over two visits to prevent fatigue, and the second measurements were always within a month of the first and at the same time of day. Measured changes outside this range are considered to reflect real clinical changes. Table A1

lists the mean differences, standard deviations, upper LoAs with CIs, and lower LoAs with CIs of the test and re-test measurements for all photopic and mesopic functions. In figures A1, A2, A3 and A4, agreements between the test and retest of all photopic and mesopic measurements are illustrated in Bland-Altman plots. The points of the difference distribution are symmetrically distributed about the mean differences which indicates that the repeated VA and FCS in both light conditions show random variability.

	Mean Difference ±SD	Upper LoA (confidence interval)	Lower LoA (confidence interval)
Photopic negative contrast VA monocular	-0.02 ± 0.09	0.15 (0.12 to 0.22)	-0.19 (-0.15 to -0.26)
Photopic positive contrast VA monocular	0.01 ± 0.10	0.20 (0.16 to 0.28)	-0.18 (-0.138 to -0.256)
Photopic negative contrast VA binocular	-0.01 ± 0.08	0.14 (0.11 to 0.21)	-0.17 (-0.14 to -0.23)
Photopic positive contrast VA binocular	0.02 ± 0.09	0.20 (0.17 to 0.28)	-0.17 (-0.13 to -0.24)
Photopic negative contrast FCS monocular	0.02 ± 0.10	0.22 (0.18 to 0.30)	-0.17 (-0.13 to -0.25)
Photopic positive contrast FCS monocular	0.03 ± 0.09	0.20 (0.16 to 0.27)	-0.14 (-0.11 to -0.21)
Photopic negative contrast FCS binocular	0.01 ± 0.12	0.25 (0.20 to 0.35)	-0.24 (-0.19 to -0.34)
Photopic positive contrast FCS binocular	0.00 ± 0.13	0.26 (0.21 to 0.37)	-0.26 (-0.21 to -0.37)
Mesopic negative contrast VA monocular	- 0.02 ± 0.07	0.11 (0.08 to 0.16)	-0.15 (-0.12 to -0.20)
Mesopic positive contrast VA monocular	-0.03 ± 0.07	0.12 (0.09 to 0.18)	-0.17 (-0.14 to -0.23)
Mesopic negative contrast VA binocular	0.01 ± 0.08	0.21 (0.17 to 0.29)	-0.18 (-0.14 to -0.26)
Mesopic positive contrast VA binocular	-0.01 ± 0.06	0.12 (0.09 to 0.17)	-0.17 (-0.10 to -0.18)
Mesopic negative contrast FCS monocular	0.03 ± 0.10	0.23 (0.19 to 0.32)	-0.17 (-0.13 to -0.25)
Mesopic positive contrast FCS monocular	0.01 ± 0.11	0.22 (0.17 to 0.30)	-0.20 (-0.16 to -0.29)
Mesopic negative contrast FCS binocular	0.02 ± 0.08	0.19 (0.15 to 0.25)	-0.14 (-0.11 to -0.21)
Mesopic positive contrast FCS binocular	0.00 ± 0.15	0.29 (0.23 to 0.41)	-0.28 (-0.22 to -0.40)

Table A1 Mean differences, standard deviations, upper limits of agreement with confidence intervals and lower limits of agreement with confidence intervals of each monocular and binocular VA and FCS measurements in photopic and mesopic conditions.

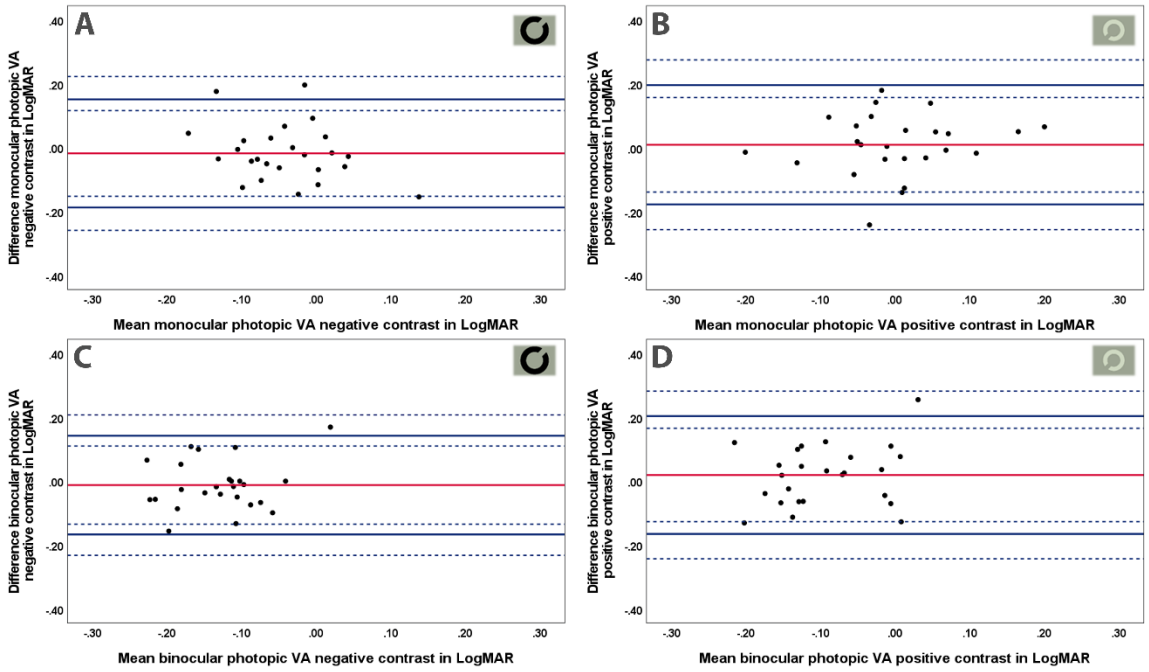


Figure A1 Bland-Altman plots obtained in the repeatability study of photopic monocular VA negative contrast (A), photopic monocular VA positive contrast (B), photopic binocular VA negative contrast (C) and photopic binocular VA positive contrast (D). In each graph the red solid line represents the average of the difference, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

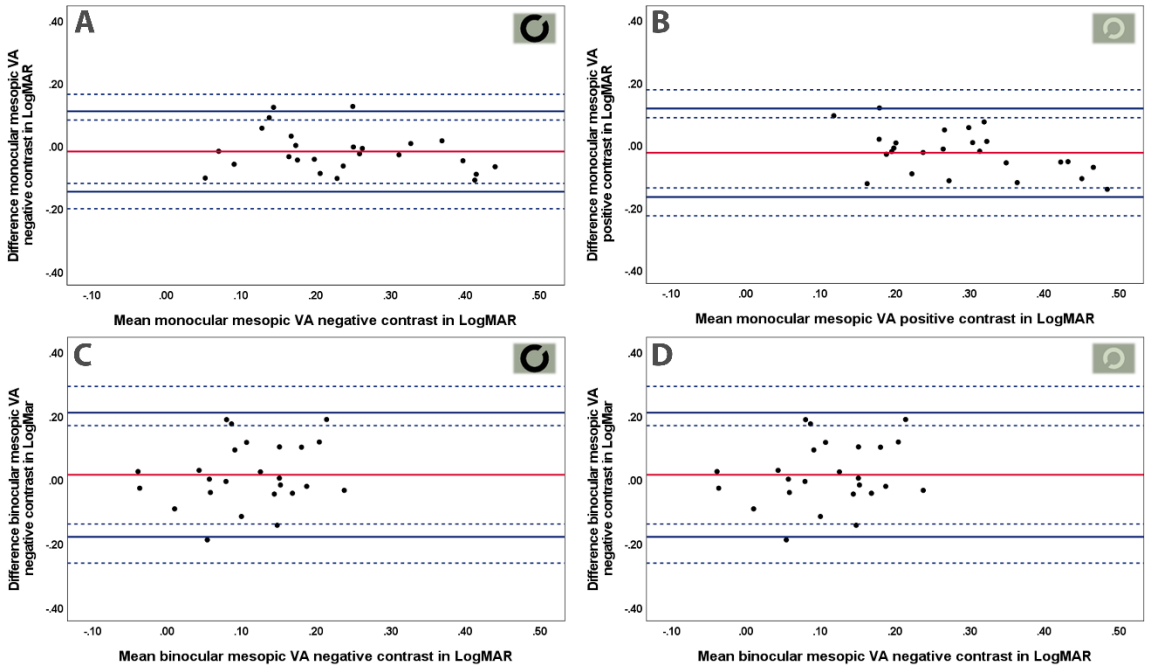


Figure A2 Bland-Altman plots obtained in the repeatability study of mesopic monocular VA negative contrast (A), mesopic monocular VA positive contrast (B), mesopic binocular VA negative contrast (C) and mesopic binocular VA positive contrast (D). In each graph the red solid line represents the average of the difference, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

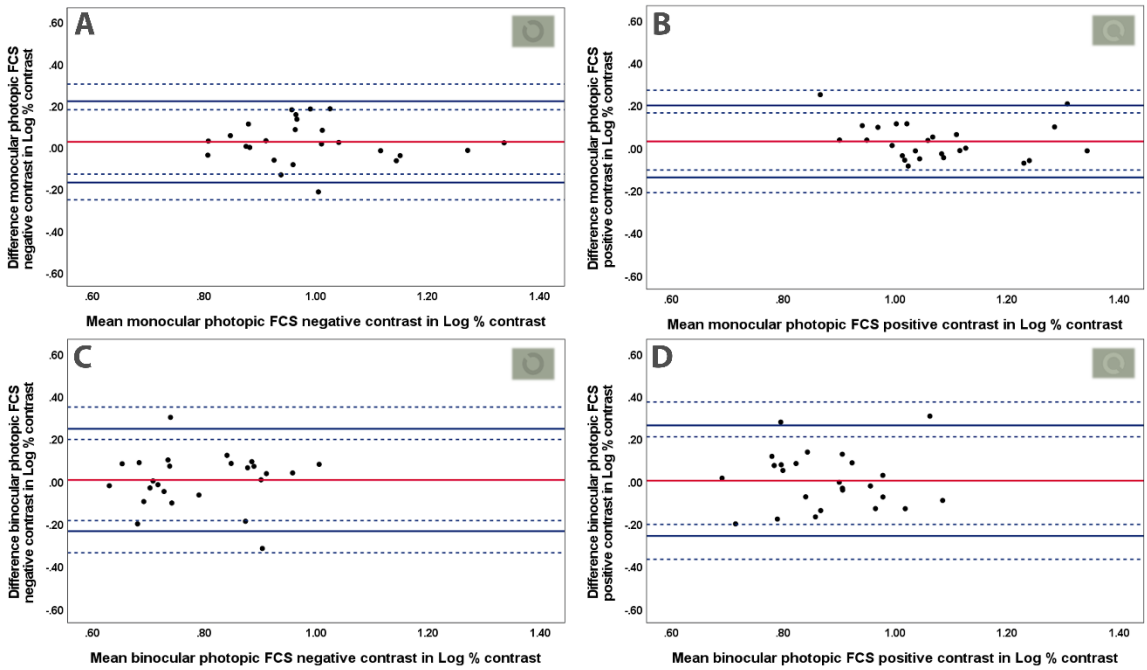


Figure A3 Bland-Altman plots obtained in the repeatability study of photopic monocular FCS negative contrast (A), photopic monocular FCS positive contrast (B), photopic binocular FCS negative contrast (C) and photopic binocular FCS positive contrast (D). In each graph the red solid line represents the average of the difference, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

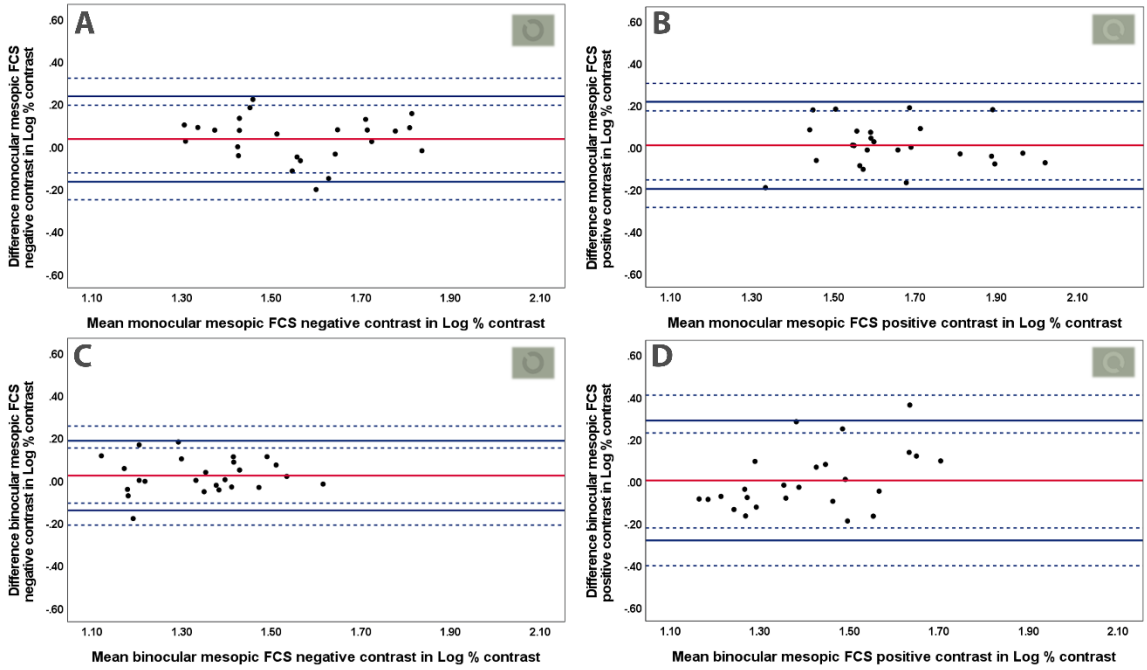


Figure A4 Bland-Altman plots obtained in the repeatability study of mesopic monocular FCS negative contrast (A), mesopic monocular FCS positive contrast (B), mesopic binocular FCS negative contrast (C) and mesopic binocular FCS positive contrast (D). In each graph the red solid line represents the average of the difference, the blue solid lines represent the 95% limits of agreement and the blue dashed lines the confidence intervals for the limits of agreement.

Discussion

The difference between two measurements with the same test, would be zero in the ideal situation. However, in practice, the pursuit is to find results close to zero. Reliability of repeated measurements were assessed by Bland-Altman plots, which describes agreement between two quantitative measurements and are an appropriate type of analysis as they directly indicate within-participant variability. The mean differences of photopic VA and FCS measurements are close to zero with an absence of marked variability increase across the acuity and contrast ranges covered. Acceptable limits must be defined by the application of the test in clinical practice or for research purposes. The Bland-Altman plots only estimate them, and the acceptability depends on the application (Giavarina, 2015). In the early detection of suspicious VA and FCS thresholds in photopic and mesopic light conditions, the determined LoAs are acceptable. If VA and FCS results are borderline, repeating the measurement may be considered. In this study, participants were included across a wide age range. It would be of interest to investigate if the repeatability is affected by age with more participants per age group. An increase of the sample size will also result in CIs closer to the LoAs. Furthermore, the effect of learning cannot be entirely excluded. All the participants were tested twice, and learning effects in ophthalmic examinations are important (Hong et al., 2007; Heijl, Lindgren and Olsson, 1989; Pierre-Filho et al., 2010).
Unpublished preliminary exploratory data of frequent repetitions of one VA or FCS measurement showed good agreement. It would be of interest to include an adequate number of participants and investigate the repeatability based on multiple repetitions. The repeatability of the VA and FCS measurements in both light conditions and contrast polarities were conducted in healthy participants with normal visual performance. To establish the repeatability in participants suffering systemic diseases with ocular involvement or ocular conditions, an adequate number of participants for a specific condition need to be included.

Conclusions

For the screening purposes of the Acuity-*Plus* test, the repeatability results of the photopic and mesopic VA and FCS in both polarities are good. Further investigations are needed to show how these results are related to patients with ocular conditions or systemic disease that can affect the eyes.

Recommendations for future work

It would be of interest to determine the test retest repeatability in patients with ocular disease and systemic disease that can affect the eye. In this study, each participant was tested twice. Multiple repetitions of one specific measurement may contribute to exclude the effect of learning effect. The results in this study didn't show marked differences between the different ages. However, the Acuity-*Plus* test is a computer based test, and repeatability may differ between younger and older participants. This can be investigated by including more participants for each age group.

Appendix B: Information sheet participants 16-90 years location Damme Optometrie

CITY UNIVERSITY LONDON

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Tait Building,
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Fax: +44 20 70408355
www.city.ac.uk/avrc

John L Barbur	Director & Head of Colour Vision Laboratory
Chris Hull	Head of Division of Optometry & Visual Science
David Crabb	Head of Applied Vision Group
Ron Douglas	Head of Visual Neuroscience

INFORMATION SHEET

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

This information sheet provides information for people who are considering participation in our study. The information here is intended for potential adult participants or the parents/guardians of potential minor participants. The term "you" refers to the minor or adult who is considering participation. For minors, a separate letter is provided for their own information.

Invitation

We would like to invite you to take part in a research study carried out at Damme Optometrie, Kesteren in conjunction with City University London. Before you decide whether you want to take part in this study you should read this information sheet carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can also contact an independent advisor for advice. They will answer your questions in an unbiased fashion, their details can be found on page 4.

1. **What is the purpose of the study?**

The purpose of the study is to establish how our vision changes under different lighting conditions (normal daylight and at night) in healthy people with normal vision and also in people with different diseases such as Diabetes and Glaucoma. The results of the study will allow a better understanding of our vision under different light levels and how different diseases may affect this.

2. What will happen if I take part?

As part of this investigation we will ask you questions about your eyes and general health, and check your spectacle prescription. We will also test the health of the front and back of your eyes and take a photograph of the back of your eyes. In addition we will check your vision using the acuity plus test in different lighting conditions. This is a computerised test carried out at 3 meters and requires judgements about the location of the gap in the letter C (Fig. 1). In the case of minors, especially children under the age of 15, we will ask the parent/guardian to be present during the examination.

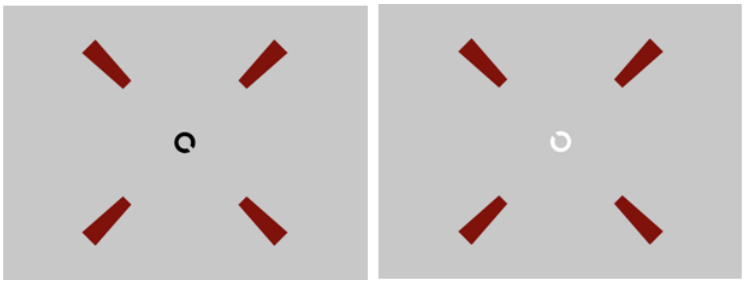

Figure 1 Examples of possible test figures

3. What do we expect from you?

One visit of approximately one hour duration to Damme Optometrie , Kesteren. Breaks will be provided as and when required.

4. What are the possible benefits and disadvantages/risks of taking part?

Although these procedures may give you useful information about your vision, they are not a full eye test that can be used for diagnostic purposes, and are no substitute for regular visits to your optometrist. We will inform you if any abnormalities are identified during the tests, and refer to the appropriate specialist (general practitioner, ophthalmologist). None of the tests are part of a treatment and are only used in the diagnosis of eye abnormalities. All tests are safe and we know no possible risk of taking part in this study.

5. What if I do not want to take part in this study?

Participation in this study is voluntary, it is your own decision to take part. You are free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or decision not to take part, will not affect you in any way. In case of minors,

the parents or legal guardians are able to withdraw their child from the study. The researcher may decide to withdraw a participant from the study if needed.

6. What will happen when the research study has ended?

We may publish the results of this study in a scientific journal or present the results at a scientific conference or a seminar in a university. The results may also be published on the website of City University London. We would be happy to discuss the results of the study with you and to send to send you a copy of the results. It will not be possible to identify you in any report or publication.

7. Am I insured when I take part in this study?

The study is insured by City University London.

8. What will happen with your information?

All information that is collected about you during the course of the research will be kept strictly confidential. All data will be anonymised, only a code is attached to your file. Identification is only possible with the identification-code list which will be safely locked in a cabinet. Only the researchers of this study have access to the identification-code list. It will not be possible to identify yourself or your results in any report or publication.

It is obligatory to keep the results of the study for 15 years. After 15 years all the data will be irreversibly destroyed.

9. Will your general practitioner and/or specialist be informed?

Your general practitioner and/or specialist will not be informed about your participation in this study. However, if there are any abnormalities identified during the tests, you will be informed and referred to the appropriate specialist (general practitioner, ophthalmologist) if needed.

10. Will I be paid to take part in the study?

No, you will not receive any expenses or compensation for participating in the study. If applicable you will be issued with an updated prescription.

11. Which medical ethical committee has approved this study?

This study have been considered and approved by the Research and Ethical Committee at City University London and the medical ethical committee (METC) of

University Medical Center Utrecht. You can find more information about the approval in the general brochure of the medical research involving human subjects.

12. Further information and contact details

If you have any questions, before, during or after the study, or need more information, please contact the researcher using the contact details given below.

Arjan Keuken, MSc optometrist
Damme Optometrie
Hoofdstraat 28
4041 AD Kesteren
Tel. [redacted]
E-mail: [redacted]

13. Independent advice

If you want independent advice about participation in this study, please contact our independent expert, using the contact details given below.

Henk Stam, BOptom, FAAO
Bartiméus Amsterdam
Osdorperban 11a
1068 LD Amsterdam
Tel. [redacted]
E-mail: [redacted]

14. Complaint procedures

If there is any aspect of the study which concerns you, you can make a complaint. City University London has established a complaints procedure via the Secretary to the University's Senate Research Ethics Committee. To complain about the study, you need to phone: 0044 (0) 20 7040 3040. You can ask to speak to the Secretary of the Senate Research Ethics Committee and inform them the name of the project is: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

You could also write to the Secretary at:

Anna Ramberg
Secretary to Senate Research Ethics Committee
CRIDO
City University
Northampton Square

London
EC1V 0HB
E-mail: Anna.Ramberg.1@city.ac.uk

Thank you for reading the information sheet. If there are any questions, please contact the researcher. We hope you are willing to take part in this study.
If, after careful consideration, you decide to participate in this study, we ask you to complete the consent form.

Signing consent form

Name, date and signature participant and researcher on informed consent:

- From the age of 16 years: signature by participant
- Child younger than 12 years: signature by both parents/guardian
- Child between 12 and 16 years old: signature by child and both parents/guardian

Appendix C: Consent form participants 16-90 years location Damme Optometrie

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John L Barbur	Director & Head of Colour Vision Laboratory
Chris Hull	Head of Division of Optometry & Visual Science
David Crabb	Head of Applied Vision Group
Ron Douglas	Head of Visual Neuroscience

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have read the participant information sheet. I understand the nature and demands of the research study that has been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to my information.

I understand that that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep my results for 15 years after the study is ended.

I agree to take part in this study.

Name participant:
Signature: Date : __ / __ / __

-

I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-

Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

Appendix D: Information sheet participants 12-15 years location Damme Optometrie

CITY UNIVERSITY LONDON

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John L Barbur — Director & Head of Colour Vision Laboratory
Chris Hull — Head of Division of Optometry & Visual Science
David Crabb — Head of Applied Vision Group
Ron Douglas — Head of Visual Neuroscience

INFORMATION SHEET (12-15 years)

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

Invitation

We would like to invite you to take part in a research study. Research is the way we find out answers to questions. This study will be carried out at Damme Optometrie, Kesteren in conjunction with City University London.

Before you decide whether you want to take part in this study you should read this sheet and discuss it with your parents/legal guardian. Your parents/legal guardian will also receive an information sheet with detailed information about this study. Ask us if there is anything that is not clear or if you would like more information. You can also contact an independent advisor for advice. Their details can also be found on page 3 and 4.

2. What is the purpose of the study?

The purpose of the study is to establish how our vision changes under different lighting conditions (normal daylight and at night) in people with good vision and people with diseases such as high blood pressure. The results of the study will allow a better understanding of our vision under different light levels and how different diseases may affect this.

2. What will happen if I take part?

As part of this investigation we will ask you questions about your eyes and general health, and check your spectacle prescription. We will also test the health of the front and back of your eyes and take a photograph of the back of your eyes. In addition we will check how well you see using the acuity plus test in different lighting conditions. The test is like a simple computer game and requires you to tell us where the gap in the letter C is(Fig. 1). Your parent/guardian will be asked to be present during the examination, especially when you are younger than 15 years.

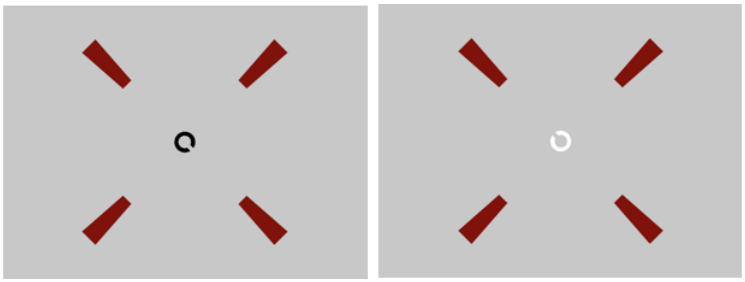

Figure 1 Examples of possible test figures

5. What do we expect from you?

One visit of approximately one hour duration to Damme Optometrie, Kesteren.. The tests will normally last an hour and you can take as many breaks as you like.

6. What are the possible benefits and disadvantages/risks of taking part?

Although these procedures may give you useful information about your vision, they are not a full eye test that can be used for diagnostic purposes, and are no substitute for regular visits to your optometrist. We will inform you, and your parents/legal guardian, if we find any abnormalities during the tests, and refer to the general practitioner or ophthalmologist if needed. All tests are safe and we know no possible risk of taking part in this study.

5. What if I do not want to take part in this study?

Participation in this study is voluntary. If you decide to take part you should discuss this with your parents/guardian. Consent of your parents/legal guardian is needed if you are minor. If you decide not to take part, you do not have to do anything. You do not have to explain why. You are free to stop at any time, without giving a reason. A decision to stop at any time, or decision not to take part, will not affect you in any way. Your parents/legal guardian can also withdraw you from this study if they feel that it is in your best interests not to take part. The researcher may decide to withdraw you from the study if needed.

6. What will happen when the research study has ended?

We may publish or present the results of this study. The results may also be published on the website of City University London. We would be happy to discuss the results of the study with you, and your parents/legal guardian, and to send you a copy of the results. In all reports and publications information is anonymised. That is to say, no identifiable information such as name, birth date, address will be used.

7. Am I insured when I take part in this study?

The study is insured by City University London.

8. What will happen with your information?

It will not be possible to identify yourself or your results in any report or publication. Your name, address and birth date will not be used. The results will be kept for 15 years and irreversibly destroyed after this period.

9. Will your general practitioner and/or specialist be informed?

Your general practitioner and/or specialist will not be informed about your participation in this study. However, if we find any abnormalities during the tests, you, and your parents/legal guardian, will be informed and referred to the appropriate specialist (general practitioner, ophthalmologist) if needed.

11. Will I be paid to take part in the study?

No, you will not receive any expenses or compensation for participating in the study. If applicable you will be issued with an updated prescription.

12. Which medical ethical committee has checked this study?

This study have been checked and accepted by the Research and Ethical Committee at City University London and the medical ethical committee (METC) of University Medical Center Utrecht.

12. Further information and contact details

If you have any questions, before, during or after the study, or need more information, please contact the researcher using the contact details given below.

Arjan Keuken, MSc optometrist
Damme Optometrie
Hoofdstraat 28

4041 AD Kesteren
Tel. [redacted]
E-mail: [redacted]

13. Independent advice

If you want independent advice about participation in this study, please contact our independent expert, using the contact details given below.

Henk Stam, BOptom, FAAO
Bartiméus Amsterdam
Osdorperban 11a
1068 LD Amsterdam
Tel. [redacted]
E-mail: [redacted]

14. Complaint procedures

If there is any aspect of the study which concerns you, you can make a complaint. City University London has established a complaints procedure via the Secretary to the University's Senate Research Ethics Committee. To complain about the study, you need to phone: 0044 (0) 20 7040 3040. You can ask to speak to the Secretary of the Senate Research Ethics Committee and inform them the name of the project is: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

You could also write to the Secretary at:

Anna Ramberg
Secretary to Senate Research Ethics Committee
CRIDO
City University
Northampton Square
London
EC1V 0HB
E-mail: Anna.Ramberg.1@city.ac.uk

Thank you for reading the information sheet. If there are any questions, please do not hesitate to contact the researcher. We hope you are willing to take part in this study.

If, after careful consideration, you decide to participate in this study, we ask you to complete the consent form.

Signing consent form

Name, date and signature participant and researcher on informed consent:

- From the age of 16 years: signature by participant
- Child younger than 12 years: signature by both parents/guardian
- Child between 12 and 16 years old: signature by child and both parents/guardian

Appendix E: Consent form participants 12-15 years location Damme Optometrie

CITY UNIVERSITY LONDON

Applied Vision Research Centre
The Henry Wellcome Laboratories for Vision Sciences
City University

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

John L Barbur	Director & Head of Colour Vision Laboratory
Chris Hull	Head of Division of Optometry & Visual Science
David Crabb	Head of Applied Vision Group
Ron Douglas	Head of Visual Neuroscience

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have read the participant information sheet. I understand the nature and demands of the research study that has been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to my information.

I understand that that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep my results for 15 years after the study is ended.

I agree to take part in this study.

Name participant:
Signature: Date : __ / __ / __

-
I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-
Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

-

CITY UNIVERSITY LONDON

Applied Vision Research Centre
The Henry Wellcome Laboratories for Vision Sciences
City University

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www.city.ac.uk/avrc

John L Barbur — Director & Head of Colour Vision Laboratory
Chris Hull — Head of Division of Optometry & Visual Science
David Crabb — Head of Applied Vision Group
Ron Douglas — Head of Visual Neuroscience

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have been asked to give consent, so that my child can participate in this study.

Name of participant: Date of birth: __ / __ / __

I have read the participant information sheet. I understand the nature and demands of the research study that have been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation of my child is voluntary and that I am free to withdraw my child at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to the information of my child.

I understand that that any information about my child is confidential, and that no information that could lead to the identification of my child will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep the results of my child for 15 years after the study is ended.

I agree that my child takes part in this study.

Name parent/legal guardian:
Signature: Date: __ / __ / __
Name parent/Legal guardian:
Signature: Date: __ / __ / __

I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

Appendix F: Information sheet participants 10-11 years location Damme Optometrie

CITY UNIVERSITY LONDON

Applied Vision Research Centre
The Henry Wellcome Laboratories for Vision Sciences
City University

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

John L Barbur — Director & Head of Colour Vision Laboratory
Chris Hull — Head of Division of Optometry & Visual Science
David Crabb — Head of Applied Vision Group
Ron Douglas — Head of Visual Neuroscience

INFORMATION SHEET (10-11 years)

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

What is research?

Research is the way we find out answers to questions. We are asking if you will help us with this piece of research.

Who are we?

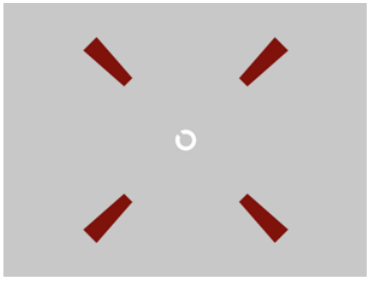
We are a group of researchers who are interested in vision in daylight and in dark.

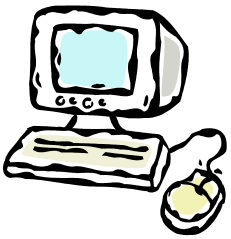
Do you have to say yes?

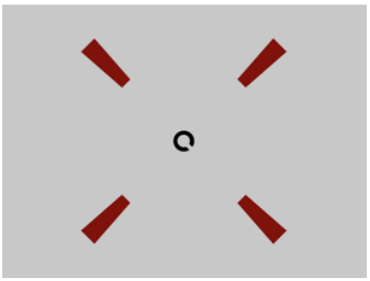
It is completely up to you and your family to decide whether to say yes or no to helping with our research. Your family will also receive an information sheet with detailed information of this research.

What will happen if you do say yes?

We will check the health of your eyes and measure your vision in daylight and in the dark. We will use a special test called the acuity plus test. You will be asked to look at a computer screen at 3 meters and will need to choose the right location of the gap in the letter C (see figures below). The test is like a simple computer game. Your parent/guardian will be present during the examinations.

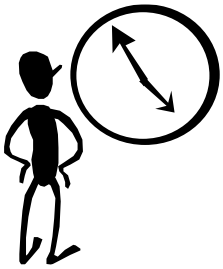






How long will it take?

It will take about one hour in total. All the tests will be carried out in one visit. During the tests you can take as many breaks as you want.



What happens afterwards?

We will look at the results from you and all of the people who are part of our study. We will not use your name, so it is not possible to find your name in any of the reports. We can send you and your family a letter with the results of this study.

Before any research is allowed to happen it has been checked out by a group of people called a Research Ethics Committee. This study has been checked and accepted by the School of Community and Health Sciences Research Ethics Committee at City University, London and the Medical Ethical Committee of University Medical Center Utrecht.

If you have any questions?

You can contact the researcher if you have any questions about this study:

Arjan Keuken
Damme Optometrie
Hoofdstraat 28
4041 AD Kesteren

Telephone: [redacted]

E-mail: [redacted]

Appendix G: Consent form participants 10-11 years location Damme Optometrie

CITY UNIVERSITY LONDON

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Fax: +44 20 70408355
www.city.ac.uk/avrc

John L Barbur — Director & Head of Colour Vision Laboratory
Chris Hull — Head of Division of Optometry & Visual Science
David Crabb — Head of Applied Vision Group
Ron Douglas — Head of Visual Neuroscience

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have been asked to give consent, so that my child can participate in this study.

Name of participant: Date of birth: __ / __ / __

I have read the participant information sheet. I understand the nature and demands of the research study that have been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation of my child is voluntary and that I am free to withdraw my child at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to the information of my child.

I understand that that any information about my child is confidential, and that no information that could lead to the identification of my child will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep the results of my child for 15 years after the study is ended.

I agree that my child takes part in this study.

Name parent/legal guardian:
Signature: Date: __ / __ / __
Name parent/Legal guardian:
Signature: Date: __ / __ / __

I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

Appendix H: Information sheet participants 16-90 years location University of Applied Sciences, Utrecht

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

INFORMATION SHEET

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

This information sheet provides information for people who are considering participation in our study. The information here is intended for potential adult participants or the parents/guardians of potential minor participants. The term "you" refers to the minor or adult who is considering participation. For minors, a separate letter is provided for their own information.

Invitation

We would like to invite you to take part in a research study carried out at University of Applied Sciences, Utrecht and Damme Optometrie, Kesteren in conjunction with City University London. Before you decide whether you want to take part in this study you should read this information sheet carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can also contact an independent advisor for advice. They will answer your questions in an unbiased fashion, their details can be found on page 4.

3. What is the purpose of the study?

The purpose of the study is to establish how our vision changes under different lighting conditions (normal daylight and at night) in healthy people with normal vision and also in people with different diseases such as Diabetes and Glaucoma. The results of the study will allow a better understanding of our vision under different light levels and how different diseases may affect this.

2. What will happen if I take part?

As part of this investigation we will ask you questions about your eyes and general health, and check your spectacle prescription. We will also test the health of the front and back of your eyes and take a photograph of the back of your eyes. In addition we will check your vision using the acuity plus test in different lighting conditions. This is a computerised test carried out at 3 meters and requires judgements about the location of the gap in the letter C (Fig. 1). In the case of minors, especially children under the age of 15, we will ask the parent/guardian to be present during the examination.

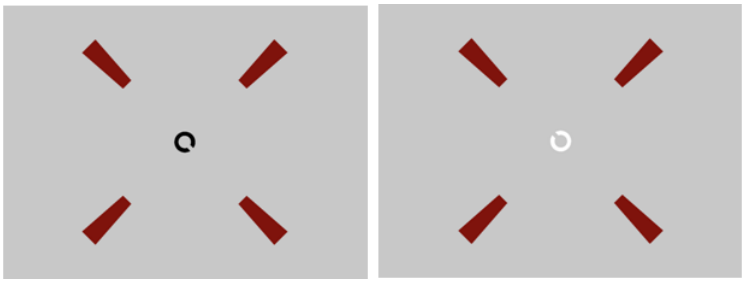

Figure 1 Examples of possible test figures

7. What do we expect from you?

One visit of approximately one hour duration to the optometry university clinic of University of Applied Sciences, Utrecht. Breaks will be provided as and when required.

8. What are the possible benefits and disadvantages/risks of taking part?

Although these procedures may give you useful information about your vision, they are not a full eye test that can be used for diagnostic purposes, and are no substitute for regular visits to your optometrist. We will inform you if any abnormalities are identified during the tests, and refer to the appropriate specialist (general practitioner, ophthalmologist). None of the tests are part of a treatment and are only used in the diagnosis of eye abnormalities. All tests are safe and we know no possible risk of taking part in this study.

5. What if I do not want to take part in this study?

Participation in this study is voluntary, it is your own decision to take part. You are free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or decision not to take part, will not affect you in any way. In case of minors, the parents or legal guardians are able to withdraw their child from the study. The researcher may decide to withdraw a participant from the study if needed.

8. What will happen when the research study has ended?

We may publish the results of this study in a scientific journal or present the results at a scientific conference or a seminar in a university. The results may also be published on the website of City University London. We would be happy to discuss the results of the study with you and to send to send you a copy of the results. It will not be possible to identify you in any report or publication.

9. Am I insured when I take part in this study?

The study is insured by City University London.

8. What will happen with your information?

All information that is collected about you during the course of the research will be kept strictly confidential. All data will be anonymised, only a code is attached to your file. Identification is only possible with the identification-code list which will be safely locked in a cabinet. Only the researchers of this study have access to the identification-code list. It will not be possible to identify yourself or your results in any report or publication.

It is obligatory to keep the results of the study for 15 years. After 15 years all the data will be irreversibly destroyed.

9. Will your general practitioner and/or specialist be informed?

Your general practitioner and/or specialist will not be informed about your participation in this study. However, if there are any abnormalities identified during the tests, you will be informed and referred to the appropriate specialist (general practitioner, ophthalmologist) if needed.

13. Will I be paid to take part in the study?

No, you will not receive any expenses or compensation for participating in the study. If applicable you will be issued with an updated prescription.

14. Which medical ethical committee has approved this study?

This study have been considered and approved by the Research and Ethical Committee at City University London and the medical ethical committee (METC) of University Medical Center Utrecht. You can find more information about the approval in the general brochure of the medical research involving human subjects.

12. Further information and contact details

If you have any questions, before, during or after the study, or need more information, please contact the researcher using the contact details given below.

Arjan Keuken, MSc optometrist
Optometry Clinic, University of Applied Sciences
Bolognalaan 101
3584 CJ Utrecht (Uithof)
Tel. [redacted]
E-mail: [redacted]

15. Independent advice

If you want independent advice about participation in this study, please contact our independent expert, using the contact details given below.

Henk Stam, BOptom, FAAO
Bartiméus Amsterdam
Osdorperban 11a
1068 LD Amsterdam
Tel. [redacted]
E-mail: [redacted]

16. Complaint procedures

If there is any aspect of the study which concerns you, you can make a complaint. City University London has established a complaints procedure via the Secretary to the University's Senate Research Ethics Committee. To complain about the study, you need to phone: 0044 (0) 20 7040 3040. You can ask to speak to the Secretary of the Senate Research Ethics Committee and inform them the name of the project is: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.
You could also write to the Secretary at:

Anna Ramberg
Secretary to Senate Research Ethics Committee
CRIDO
City University
Northampton Square
London
EC1V 0HB

E-mail: Anna.Ramberg.1@city.ac.uk

Thank you for reading the information sheet. If there are any questions, please contact the researcher. We hope you are willing to take part in this study.
If, after careful consideration, you decide to participate in this study, we ask you to complete the consent form.

Signing consent form

Name, date and signature participant and researcher on informed consent:

- From the age of 16 years: signature by participant
- Child younger than 12 years: signature by both parents/guardian
- Child between 12 and 16 years old: signature by child and both parents/guardian

Appendix I: Consent form participants 16-90 years location University of Applied Sciences, Utrecht

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have read the participant information sheet. I understand the nature and demands of the research study that has been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to my information.

I understand that that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep my results for 15 years after the study is ended.

I agree to take part in this study.

Name participant:
Signature: Date : __ / __ / __

-
I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-
Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

-

Appendix J: Information sheet participants 12-15 years location University of Applied Sciences, Utrecht

CITY UNIVERSITY LONDON

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London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

INFORMATION SHEET (12-15 years)

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

Invitation

We would like to invite you to take part in a research study. Research is the way we find out answers to questions. This study will be carried out at University of Applied Sciences, Utrecht and Damme Optometrie, Kesteren in conjunction with City University London.

Before you decide whether you want to take part in this study you should read this sheet and discuss it with your parents/legal guardian. Your parents/legal guardian will also receive an information sheet with detailed information about this study. Ask us if there is anything that is not clear or if you would like more information. You can also contact an independent advisor for advice. Their details can also be found on page 3 and 4.

4. What is the purpose of the study?

The purpose of the study is to establish how our vision changes under different lighting conditions (normal daylight and at night) in people with good vision and people with diseases such as high blood pressure. The results of the study will allow a better understanding of our vision under different light levels and how different diseases may affect this.

2. What will happen if I take part?

As part of this investigation we will ask you questions about your eyes and general health, and check your spectacle prescription. We will also test the health of the front and back of your eyes and take a photograph of the back of your eyes. In addition we will check how well you see using the acuity plus test in different lighting conditions. The test is like a simple computer game and requires you to tell us where the gap in the letter C is(Fig. 1). Your parent/guardian will be asked to be present during the examination, especially when you are younger than 15 years.

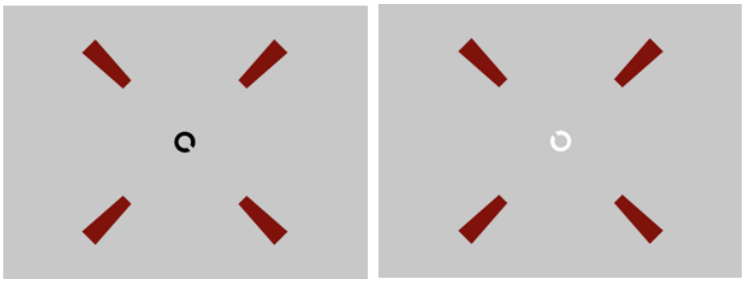


Figure 1 Examples of possible test figures

9. What do we expect from you?

One visit of approximately one hour duration to the optometry university clinic of University of Applied Sciences, Utrecht. The tests will normally last an hour and you can take as many breaks as you like.

10. What are the possible benefits and disadvantages/risks of taking part?

Although these procedures may give you useful information about your vision, they are not a full eye test that can be used for diagnostic purposes, and are no substitute for regular visits to your optometrist. We will inform you, and your parents/legal guardian, if we find any abnormalities during the tests, and refer to the general practitioner or ophthalmologist if needed. All tests are safe and we know no possible risk of taking part in this study.

5. What if I do not want to take part in this study?

Participation in this study is voluntary. If you decide to take part you should discuss this with your parents/guardian. Consent of your parents/legal guardian is needed if you are minor. If you decide not to take part, you do not have to do anything. You do not have to explain why. You are free to stop at any time, without giving a reason. A decision to stop at any time, or decision not to take part, will not affect you in any way. Your parents/legal guardian can also withdraw you from this study if they feel

that it is in your best interests not to take part. The researcher may decide to withdraw you from the study if needed.

7. What will happen when the research study has ended?

We may publish or present the results of this study. The results may also be published on the website of City University London. We would be happy to discuss the results of the study with you, and your parents/legal guardian, and to send you a copy of the results. In all reports and publications information is anonymised. That is to say, no identifiable information such as name, birth date, address will be used.

8. Am I insured when I take part in this study?

The study is insured by City University London.

8. What will happen with your information?

It will not be possible to identify yourself or your results in any report or publication. Your name, address and birth date will not be used. The results will be kept for 15 years and irreversibly destroyed after this period.

10. Will your general practitioner and/or specialist be informed?

Your general practitioner and/or specialist will not be informed about your participation in this study. However, if we find any abnormalities during the tests, you, and your parents/legal guardian, will be informed and referred to the appropriate specialist (general practitioner, ophthalmologist) if needed.

15. Will I be paid to take part in the study?

No, you will not receive any expenses or compensation for participating in the study. If applicable you will be issued with an updated prescription.

16. Which medical ethical committee has checked this study?

This study have been checked and accepted by the Research and Ethical Committee at City University London and the medical ethical committee (METC) of University Medical Center Utrecht.

12. Further information and contact details

If you have any questions, before, during or after the study, or need more information, please contact the researcher using the contact details given below.
Arjan Keuken, MSc optometrist

Optometry Clinic, University of Applied Sciences
Bolognalaan 101
3584 CJ Utrecht (Uithof)
Tel. [redacted]
E-mail: [redacted]

14. Independent advice

If you want independent advice about participation in this study, please contact our independent expert, using the contact details given below.

Henk Stam, BOptom, FAAO
Bartiméus Amsterdam
Osdorperban 11a
1068 LD Amsterdam
Tel. [redacted]
E-mail: [redacted]

14. Complaint procedures

If there is any aspect of the study which concerns you, you can make a complaint. City University London has established a complaints procedure via the Secretary to the University's Senate Research Ethics Committee. To complain about the study, you need to phone: 0044 (0) 20 7040 3040. You can ask to speak to the Secretary of the Senate Research Ethics Committee and inform them the name of the project is: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

You could also write to the Secretary at:

Anna Ramberg
Secretary to Senate Research Ethics Committee
CRIDO
City University
Northampton Square
London
EC1V 0HB
E-mail: Anna.Ramberg.1@city.ac.uk

Thank you for reading the information sheet. If there are any questions, please do not hesitate to contact the researcher. We hope you are willing to take part in this study.
If, after careful consideration, you decide to participate in this study, we ask you to complete the consent form.

Signing consent form

Name, date and signature participant and researcher on informed consent:

- From the age of 16 years: signature by participant
- Child younger than 12 years: signature by both parents/guardian
- Child between 12 and 16 years old: signature by child and both parents/guardian

Appendix K: Consent form participants 12-15 years location University of Applied Sciences, Utrecht

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have read the participant information sheet. I understand the nature and demands of the research study that has been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to my information.

I understand that that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep my results for 15 years after the study is ended.

I agree to take part in this study.

Name participant:
Signature: Date : __ / __ / __

-
I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-
Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have been asked to give consent, so that my child can participate in this study.

Name of participant: Date of birth: __ / __ / __

I have read the participant information sheet. I understand the nature and demands of the research study that have been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation of my child is voluntary and that I am free to withdraw my child at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to the information of my child.

I understand that that any information about my child is confidential, and that no information that could lead to the identification of my child will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep the results of my child for 15 years after the study is ended.

I agree that my child takes part in this study.

Name parent/legal guardian:
Signature: Date: __ / __ / __
Name parent/Legal guardian:
Signature: Date: __ / __ / __

-

I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-

Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

-

Appendix L: Information sheet participants 10-11 years location University of Applied Sciences, Utrecht

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

INFORMATION SHEET (10-11 years)

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

What is research?

Research is the way we find out answers to questions. We are asking if you will help us with this piece of research.

Who are we?

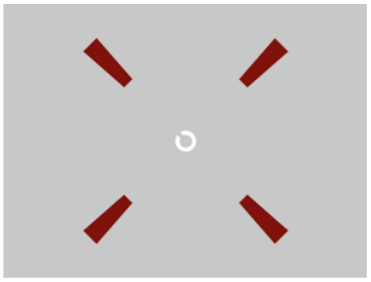
We are a group of researchers who are interested in vision in daylight and in dark.

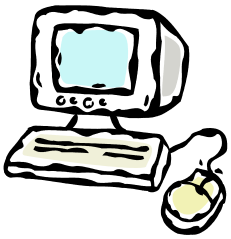
Do you have to say yes?

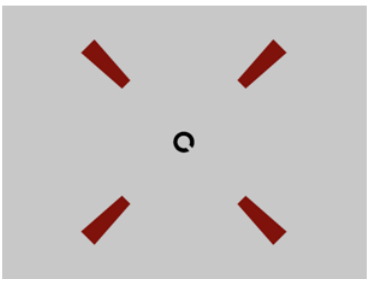
It is completely up to you and your family to decide whether to say yes or no to helping with our research. Your family will also receive an information sheet with detailed information of this research.

What will happen if you do say yes?

We will check the health of your eyes and measure your vision in daylight and in the dark. We will use a special test called the acuity plus test. You will be asked to look at a computer screen at 3 meters and will need to choose the right location of the gap in the letter C (see figures below). The test is like a simple computer game. Your parent/guardian will be present during the examinations.

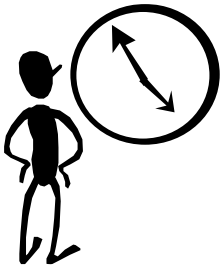






How long will it take?

It will take about one hour in total. All the tests will be carried out in one visit. During the tests you can take as many breaks as you want.



What happens afterwards?

We will look at the results from you and all of the people who are part of our study. We will not use your name, so it is not possible to find your name in any of the reports. We can send you and your family a letter with the results of this study.

Before any research is allowed to happen it has been checked out by a group of people called a Research Ethics Committee. This study has been checked and accepted by the School of Community and Health Sciences Research Ethics Committee at City University, London and the Medical Ethical Committee of University Medical Center Utrecht.

If you have any questions?

You can contact the researcher if you have any questions about this study:

Arjan Keuken
Optometry Clinic, University of Applied Sciences
Bolognalaan 101
3584 CJ Utrecht (Uithof)

Telephone: [redacted]

E-mail: [redacted]

Appendix M: Consent form participants 10-11 years location University of Applied Sciences, Utrecht

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have been asked to give consent, so that my child can participate in this study.

Name of participant: Date of birth: __ / __ / __

I have read the participant information sheet. I understand the nature and demands of the research study that have been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation of my child is voluntary and that I am free to withdraw my child at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to the information of my child.

I understand that that any information about my child is confidential, and that no information that could lead to the identification of my child will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep the results of my child for 15 years after the study is ended.

I agree that my child takes part in this study.

Name parent/legal guardian:
Signature: Date: __ / __ / __
Name parent/Legal guardian:
Signature: Date: __ / __ / __

I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

Appendix N: Information sheet participants 16-90 years location City Hall, Alphen aan den Rijn

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

INFORMATION SHEET

Title of study:

Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

This information sheet provides information for people who are considering participation in our study. The information here is intended for potential adult participants or the parents/guardians of potential minor participants. The term "you" refers to the minor or adult who is considering participation. For minors, a separate letter is provided for their own information.

Invitation

We would like to invite you to take part in a research study carried out at University of Applied Sciences, Utrecht, Damme Optometrie, Kesteren and on location for employees of City Hall Alphen aan den Rijn in conjunction with City University London. Before you decide whether you want to take part in this study you should read this information sheet carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can also contact an independent advisor for advice. They will answer your questions in an unbiased fashion, their details can be found on page 4.

5. What is the purpose of the study?

The purpose of the study is to establish how our vision changes under different lighting conditions (normal daylight and at night) in healthy people with normal vision and also in people with different diseases such as Diabetes and Glaucoma. The results of the study will allow a better understanding of our vision under different light levels and how different diseases may affect this.

2. What will happen if I take part?

As part of this investigation we will ask you questions about your eyes and general health, and check your spectacle prescription. We will also test the health of the front and back of your eyes and take a photograph of the back of your eyes. In addition we will check your vision using the acuity plus test in different lighting conditions. This is a computerised test carried out at 3 meters and requires judgements about the location of the gap in the letter C (Fig. 1). In the case of minors, especially children under the age of 15, we will ask the parent/guardian to be present during the examination.

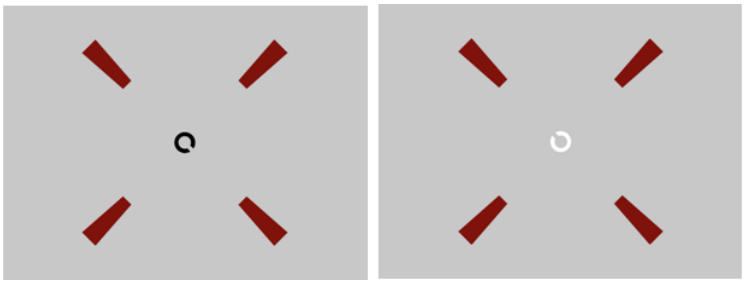


Figure 1 Examples of possible test figures

11. What do we expect from you?

One visit of approximately one hour duration in the vitality room (rear building work café VI) of City Hall Alphen aan den Rijn. Breaks will be provided as and when required.

12. What are the possible benefits and disadvantages/risks of taking part?

Although these procedures may give you useful information about your vision, they are not a full eye test that can be used for diagnostic purposes, and are no substitute for regular visits to your optometrist. We will inform you if any abnormalities are identified during the tests, and refer to the appropriate specialist (general practitioner, ophthalmologist). None of the tests are part of a treatment and are only used in the diagnosis of eye abnormalities. All tests are safe and we know no possible risk of taking part in this study.

5. What if I do not want to take part in this study?

Participation in this study is voluntary, it is your own decision to take part. You are free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or decision not to take part, will not affect you in any way. In case of minors,

the parents or legal guardians are able to withdraw their child from the study. The researcher may decide to withdraw a participant from the study if needed.

10. What will happen when the research study has ended?

We may publish the results of this study in a scientific journal or present the results at a scientific conference or a seminar in a university. The results may also be published on the website of City University London. We would be happy to discuss the results of the study with you and to send to send you a copy of the results. It will not be possible to identify you in any report or publication.

11. Am I insured when I take part in this study?

The study is insured by City University London.

8. What will happen with your information?

All information that is collected about you during the course of the research will be kept strictly confidential. All data will be anonymised, only a code is attached to your file. Identification is only possible with the identification-code list which will be safely locked in a cabinet. Only the researchers of this study have access to the identification-code list. It will not be possible to identify yourself or your results in any report or publication.

It is obligatory to keep the results of the study for 15 years. After 15 years all the data will be irreversibly destroyed.

9. Will your general practitioner and/or specialist be informed?

Your general practitioner and/or specialist will not be informed about your participation in this study. However, if there are any abnormalities identified during the tests, you will be informed and referred to the appropriate specialist (general practitioner, ophthalmologist) if needed.

17. Will I be paid to take part in the study?

No, you will not receive any expenses or compensation for participating in the study. If applicable you will be issued with an updated prescription.

18. Which medical ethical committee has approved this study?

This study have been considered and approved by the Research and Ethical Committee at City University London and the medical ethical committee (METC) of

University Medical Center Utrecht. You can find more information about the approval in the general brochure of the medical research involving human subjects.

12. Further information and contact details

If you have any questions, before, during or after the study, or need more information, please contact the researcher using the contact details given below.

Arjan Keuken, MSc optometrist
Optometry Clinic, University of Applied Sciences
Bolognalaan 101
3584 CJ Utrecht (Uithof)
Tel. [redacted]
E-mail: [redacted]

17. Independent advice

If you want independent advice about participation in this study, please contact our independent expert, using the contact details given below.

Henk Stam, BOptom, FAAO
Bartiméus Amsterdam
Osdorperban 11a
1068 LD Amsterdam
Tel. [redacted]
E-mail: [redacted]

18. Complaint procedures

If there is any aspect of the study which concerns you, you can make a complaint. City University London has established a complaints procedure via the Secretary to the University's Senate Research Ethics Committee. To complain about the study, you need to phone: 0044 (0) 20 7040 3040. You can ask to speak to the Secretary of the Senate Research Ethics Committee and inform them the name of the project is: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.
You could also write to the Secretary at:

Anna Ramberg
Secretary to Senate Research Ethics Committee
CRIDO
City University

Northampton Square
London
EC1V 0HB
E-mail: Anna.Ramberg.1@city.ac.uk

Thank you for reading the information sheet. If there are any questions, please contact the researcher. We hope you are willing to take part in this study.
If, after careful consideration, you decide to participate in this study, we ask you to complete the consent form.

Signing consent form

Name, date and signature participant and researcher on informed consent:

- From the age of 16 years: signature by participant
- Child younger than 12 years: signature by both parents/guardian
- Child between 12 and 16 years old: signature by child and both parents/guardian

Appendix O: Consent form participants 16-90 years location City Hall, Alphen aan den Rijn

CITY UNIVERSITY LONDON

Tait Building,
Northampton Square,
London EC1V 0HB.

Telephone: +44 20 70405060
Fax: +44 20 70408355
www.city.ac.uk/avrc

HOGESCHOOL UTRECHT

Title of study: Age-related normal limits for spatial vision: Separating the effects of normal ageing from changes caused by disease.

I have read the participant information sheet. I understand the nature and demands of the research study that has been explained to me and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason and without being penalized or disadvantaged in any way.

I understand that the researchers and few other people, who are mentioned in the General brochure medical research involving human subjects, have access to my information.

I understand that that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project, or to any other party. No identifiable personal data will be published.

I understand that this is a research investigation and the results cannot be used for diagnosis.

I give consent to use the information for the proposed study as explained in the information sheet.

I give consent to keep my results for 15 years after the study is ended.

I agree to take part in this study.

Name participant:
Signature: Date : __ / __ / __

-
I declare that above mentioned person/persons are fully informed about this study.

If there arises any new information during this study, that could influence the consent of the parent/legal guardian, I will inform him/her in due time.

Name researcher:
Signature: Date: __ / __ / __

-
Additional information is given by (if applicable):
Name:
Function:
Signature: Date: __ / __ / __

-

Appendix P: Abstracts congresses

Abstract oral presentation biannual OVN (Optometristen Vereniging Nederland; Dutch Optometric Association) congress on 13-2-2017 (in Dutch)

BETER LICHT OP DONKER ZIEN

Binnen de optometrie wordt veelal de visus gemeten om vast te stellen hoe iemand visueel functioneert. Het meten van contrast gevoeligheid is hiervoor ook van belang. Het komt voor dat patiënten met een uitstekende visus toch klachten ondervinden in het dagelijks leven door een lage contrast gevoeligheid. Daarnaast is het heel erg afhankelijk onder welke licht condities visus en contrastgevoeligheid worden gemeten. In de praktijk zijn problemen met zien in het donker een veelgehoorde klacht. Het is bekend dat bij verschillende oogaandoeningen de visus en contrast gevoeligheid in het bijzonder onder donkere omstandigheden verminderd is. Dit kan in een zeer vroeg stadium van de aandoening en mogelijk zelfs voordat er met klinisch onderzoek afwijkingen zichtbaar zijn. Het is echter ook bekend dat een stijging van de leeftijd, een daling in visus en contrast gevoeligheid in mesopische omstandigheden veroorzaakt. Hoe kan het effect van leeftijd gescheiden worden van het effect veroorzaakt door oogaandoeningen? City University London heeft de Acuity Plus test ontwikkeld waarmee visus en contrastgevoeligheid in photopische en mesopische omstandigheden gemeten kunnen worden. In een lopend onderzoek van City University London, wat uitgevoerd wordt bij Hogeschool Utrecht en Damme Optometrie zullen de referentie waarden van visus en contrast gevoeligheid per leeftijd worden bepaald. Hierdoor kan uiteindelijk het effect van verandering door leeftijd worden gescheiden van het effect veroorzaakt door oogaandoeningen.

Abstract oral presentation EVER 2017 (Optometristen Vereniging Nederland; Dutch Optometric Association) congress on 29-9-2017
Awarded with best paper

NORMAL UPPER AGE-LIMITS FOR PHOTOPIC AND MESOPIC VISUAL ACUITY AND FUNCTIONAL CONTRAST SENSITIVITY

A. KEUKEN[1,2], A. Subramanian[1], J.L. Barbur1.
1Applied Vision Research Centre- School of Health Sciences- City- University of London, Optometry, London, United Kingdom.
[2]University of Applied Sciences, Optometry, Utrecht, Netherlands- The.

PURPOSE
Normal, healthy aging causes a gradual worsening of vision with more pronounced effects at lower light levels (mesopic range). Normal spatial vision enables us to resolve fine spatial detail and to detect faint edges and boundaries that make up objects. Age-related changes in the optics of the eye and diseases of the retina and/or systemic diseases that affect vision can also cause a loss of spatial vision. In order to separate the latter from the effects of normal aging, reliable, upper, normal limits of spatial vision are needed for both photopic and mesopic light levels. The purpose of this investigation was to measure visual acuity (VA) and functional contrast sensitivity (FCS) as a function of age in a large sample of normal subjects and to establish reliable, statistical limits to describe normal vision.
METHODS
206 subjects (age range: 10-77 years) have been investigated. A detailed medical and ocular history and eye examination were carried out. We measured photopic and mesopic VA and FCS in each subject under binocular and monocular viewing conditions with both positive and negative contrast using the Acuity-Plus test (http://www.city.ac.uk/avot).
RESULTS
The best visual performance corresponds to ~ 15 to 35 years. The gradual increase in thresholds with increasing age was surprisingly small under all stimulus conditions below the fifth decade with significant differences between photopic and mesopic conditions.
CONCLUSIONS
Thresholds of VA and FCS increase gradually in normal aging. These preliminary results reveal a more pronounced effect between the fifth and sixth decade of life. On completion of this study, statistically-reliable, upper, normal limits for VA and FCS will be determined as a function of age. These data will make it possible to detect reliable significant loss of spatial vision that cannot be attributed to normal aging.

Abstract poster presentation ARVO 2018 (Association for Research in Vision and Ophthalmology) congress on 29-4-2018

MONOCULAR AND BINOCULAR LIMITS FOR SPATIAL VISION: EFFECTS OF 'NORMAL' AGING ON PHOTOPIC AND MESOPIC VISUAL ACUITY AND CONTRAST SENSITIVITY

Arjan Keuken[1,2], Ahalya Subramanian[1] and John L Barbur[1]

Applied Vision Research Centre[1], School of Health Sciences, City, University of London, UK.
University of Applied Sciences[2], Utrecht, Netherlands.

PURPOSE
To establish the limits of monocular and binocular spatial vision that describe only changes that can be attributed to healthy aging. To investigate the advantages of using briefly presented stimuli and mesopic light levels to detect the earliest changes in spatial vision that can be attributed to ocular or systemic disease.
METHODS
Photopic and mesopic Visual Acuity (VA) and Functional Contrast Sensitivity (FCS) were measured under binocular and monocular viewing conditions using briefly presented (180ms), Landolt-ring optotypes in negative and positive contrast. 251 subjects (age range: 10-77) participated in the study. The screening procedure included detailed medical and ocular histories and a thorough ophthalmic examination. The stimuli were generated on a high resolution visual display using the Acuity-*Plus* (AP) test developed at City, University of London. VA was also measured using a standard ETDRS test chart under photopic conditions.
RESULTS
The results reveal only a gradual increase in VA and FCS thresholds with increasing age under photopic conditions. The gap acuity of ~ 0.8 min arc measured in young subjects increases only gradually up to 50 years of age, but a larger increase of ~ 0.25 min arc / decade was observed from 50 to 80 years of age. Under mesopic conditions, these results were more pronounced. VA and FCS measured with negative contrast stimuli produced smaller and less variable thresholds. The ETDRS test chart tended to yield higher acuity for all ages and was less correlated with age when compared to the AP test.
CONCLUSIONS
VA and FCS thresholds increase gradually in normal ageing with a more rapid increase above the fifth decade. VA thresholds measured with the AP test were significantly higher and more strongly correlated with age when compared to conventional, ETDRS thresholds. Preliminary AP test data in subjects with macular disorders such as age-related macular degeneration reveal larger differences in VA thresholds when compared to ETDRS results. Our findings suggest that in addition to spatial deficits, patients with early-stage macular disease have severely impaired temporal processing. Short duration stimuli are often perceived as having reduced

spatial contrast. The AP test is therefore more sensitive in detecting vision loss in macular disease.

Abstract oral presentation biannual OVN (Optometristen Vereniging Nederland; Dutch Optometric Association) congress on 10-2-2019 (in Dutch)

CONTRASTGEVOELIGHEID METEN IN DE (OPTOMETRIE)PRAKTIJK

Het meten van de contrastgevoeligheid in de optometriepraktijk en klinische setting kan heel waardevol zijn. Deze meting levert in veel gevallen meer relevante informatie op dan een visus meting. Zeker als er ook een mogelijkheid is om de contrastgevoeligheid in mesopische omstandigheden te meten. Dit zal mede duidelijk worden gemaakt aan de hand van voorlopige resultaten van een onderzoek wat uitgevoerd wordt aan City, University of London. Bij dit onderzoek wordt gekeken wat het effect van leeftijd is op de visus en contrastgevoeligheid, zowel onder photopische als mesopische omstandigheden. Bij diverse oogaandoeningen kan de contrastgevoeligheid verminderd zijn in een zeer vroeg stadium. Het is echter van belang dit effect te scheiden van normale veranderingen als gevolg van leeftijd. Voor dit onderzoek wordt gebruik gemaakt van de Acuity Plus test. Dit is een gecomputeriseerde test waarmee visus en contrastgevoeligheid, zowel in photopische als mesopische omstandigheden gemeten kan worden.

Abstract oral presentation BCOVS 2021 (British Congress of Optometry and Vision Science) congress on 7-9-2021

AGE-RELATED NORMAL LIMITS FOR SPATIAL VISION

Arjan Keuken, MSc, Department of Optometry, University of Applied Sciences, Utrecht, Netherlands; Applied Vision Research Centre, City, University of London, London, United Kingdom
Dr. Ahalya Subramanian, PhD, Applied Vision Research Centre, City, University of London, London, United Kingdom
Dr. Sigrid Mueller-Schotte, OD, PhD, Department of Optometry, University of Applied Sciences, Utrecht, Netherlands
Prof. John Barbur, DIC, PhD, Applied Vision Research Centre, City, University of London, London, United Kingdom

PURPOSE

To establish age-related normal limits of monocular and binocular spatial vision under photopic and mesopic conditions.

METHODS

Photopic and mesopic Visual Acuity (VA) and Functional Contrast Sensitivity (FCS) were measured using both positive and negative contrast optotypes under binocular and monocular viewing conditions using the Acuity-*Plus* (AP) test. The experiments were carried out in normally sighted subjects, age-range, 10 to 86 years. Photopic VA was also measured using a standard ETDRS test chart. Participants who failed to meet pre-established, normal sight criteria were excluded from the analysis. Mean and upper normal limits (i.e., mean + 2.5σ) were calculated for each decade using best-fit, non-linear, Gauss-Newton models.

RESULTS

216 (mean age 43.1 ± 19.2) and 221 participants (mean age 44.3 ± 19.1) were included in the photopic and mesopic analysis, respectively. Photopic and mesopic thresholds for VA and FCS and overall variability were found to be age-invariant up to ~ 50 years with a gradual, but accelerating increase in both mean thresholds and inter-subject variability above this age. Results with negative contrast optotypes were significantly better than the corresponding results measured with positive contrast ($p<0.004$).

CONCLUSIONS

This project established upper normal, age limits for monocular and binocular viewing under photopic and mesopic lighting with both positive and negative contrast optotypes. A single test is needed to assess whether the patient falls within normal age-related limits. The test is sensitive to residual refractive errors, large higher-order aberrations, forward light scatter in the eye and changes in retinal sensitivity to luminance contrast.

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