A Novel Measure of Vision Competence by Assessing the Visual Acuity Space at Different Levels of Contrast and Ambient Luminance

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List of abbreviations

AFC	Alternative Forced Choice
BCVA	Best Corrected Visual Acuity
Best PEST	Best Parameter Estimation by Sequential Testing
CIE	Commission Internationale de l'Éclairage
DIN	Deutsches Institut für Normung e.V.
EN	Europäische Norm
ETDRS	Early Treatment Diabetic Retinopathy Study
FrACT	Freiburg Visual Acuity Test
ISO	International Organization for Standardization
logMAR	Logarithm of the Minimum Angle of Resolution
QUEST	Quick, Unbiased, Efficient, Statistical Tree
SEM	Standard Error of Mean
VA	Visual Acuity
VA-CAL	Visual Acuity at different levels of Contrast and Ambient Luminance
VAS	Visual Acuity Space

Summary

Visual acuity is a key parameter in the assessment of vision. It determines everyday vision, which is influenced by constantly changing contrast and lighting conditions. In clinical applications, however, these conditions are only poorly reflected by measuring visual acuity only at a single specific luminance and maximum contrast, leaving the actual visual performance under other everyday lighting conditions undetected. For this purpose, a setup has been developed that allows the presentation of optotypes at different contrasts and ambient luminance levels, the major determinants of spatial vision. In an automated test run, visual acuity was determined for a wide range of contrasts and luminance levels using an adaptive staircase algorithm and evaluated in a three-dimensional visual acuity space. The focus was on people with normal vision and patients with achromatopsia, an inherited autosomal recessive retinal disease that results in extreme sensitivity to glare and reduced visual acuity. In both cases, the standard tests of visual acuity differed enormously from their vision capabilities in daily living conditions. While the visual acuity of people with normal vision improved to a certain extent with increasing luminance, the visual acuity of people with achromatopsia dropped into range of legal blindness with increasing luminance. To counteract glare, achromatopsia patients use so-called edge filter glasses in everyday life, which alleviate their vision problems. Hence, as a further step, the benefit of these filter glasses was investigated quantitatively by measuring the visual acuity of the participants at the critical contrast luminance combinations with and without wearing the filter glass. For people with healthy eyes, this had a negative effect, as their visual acuity worsened in almost all conditions. For achromatopsia patients, the edge filter had a beneficial effect, improving their previously severe visual impairment to moderate. To quantify vision competence reflected in the visual acuity space, a new score was developed as a unified measure of vision for rapid assessment of visual acuity in daily living tasks. This score can be used as a novel endpoint to assess changes in vision competence after interventions in clinical trials. Finally, the new method and the device have been converted into a smaller version with optimized testing time for clinical use. Overall, this study presents a novel method for assessing visual acuity at different contrasts and luminance levels to provide a single measure of vision competence for typical conditions of daily living.

Zusammenfassung

Die Sehschärfe ist ein entscheidender Parameter zur Beurteilung der Sehleistung. Sie bestimmt das alltägliche Sehen, das durch ständig wechselnde Kontrast- und Lichtverhältnisse beeinflusst wird. In der klinischen Anwendung werden diese Bedingungen durch die Messung der Sehschärfe bei einer bestimmten Leuchtdichte und maximalem Kontrast jedoch nur unzureichend abgebildet, so dass die tatsächliche Sehleistung bei anderen alltäglichen Lichtverhältnissen nicht erfasst wird. Zu diesem Zweck wurde eine Apparatur entwickelt, welche die Darstellung von Sehzeichen mit verschiedenen Kontrasten und unterschiedlichen Umgebungsleuchtdichten, den wichtigsten Determinanten des räumlichen Sehens, ermöglicht. In einem automatisierten Testlauf wurde die Sehschärfe für die jeweiligen Kontraste und Leuchtdichten mittels eines adaptiven Algorithmus ermittelt und in einem dreidimensionalen Sehschärferaum evaluiert. Im Fokus standen normalsichtige Personen und Patienten mit Achromatopsie, einer autosomal-rezessiv vererbten Netzhauterkrankung, die sich insbesondere durch eine enorme Lichtempfindlichkeit und verminderte Sehschärfe äußert. In beiden Fällen wichen die Standardtests für die Sehschärfe erheblich von den Sehfähigkeiten unter Alltagsbedingungen ab. Während sich die Sehschärfe bei Normalsichtigen mit zunehmender Leuchtdichte sogar bis zu einem gewissen Grad verbesserte, fiel die Sehschärfe der Achromaten teilweise in den Bereich der gesetzlichen Blindheit. Um der Blendung entgegenzuwirken, verwenden Achromatopsie-Patienten im Alltag sogenannte Kantenfiltergläser, die ihre Sehprobleme lindern. Daher wurde weiterführend der quantitative Nutzen dieser Filtergläser untersucht, indem die Sehschärfe der Probanden unter den kritischen Bedingungen mit und ohne Filterglas gemessen wurde. Bei normalsichtigen Personen zeigte sich ein negativer Effekt, indem sich die Sehschärfe unter fast allen Bedingungen verschlechterte. Bei Achromaten wirkte sich das Tragen eines Kantenfilters nachweislich positiv aus, da sich ihre zuvor starke Sehbehinderung auf eine moderate Sehbehinderung verbesserte. Zur Quantifizierung der Sehfähigkeit, die sich im Sehschärfenraum widerspiegelt, wurde ein neuer Score als einheitliches Maß für die Sehschärfe zur schnellen Beurteilung der Sehschärfe bei Aufgaben des täglichen Lebens entwickelt. Dieser Score kann als neuartiger Endpunkt verwendet werden, um Veränderungen der Sehfähigkeit durch Behandlungen in klinischen Studien zu bewerten. Das neue Verfahren und das dazugehörige Gerät wurden

schließlich in eine mobile und zeitoptimierte Version für den klinischen Gebrauch überführt. Zusammenfassend stellt diese Studie eine neuartige Methode zur Bewertung der Sehschärfe bei verschiedenen Kontrasten und Leuchtdichten vor, die ein einziges Maß für die Sehfähigkeit unter typischen Bedingungen des täglichen Lebens liefert.

1 Introduction

This introductory chapter explains the structure and function of the human visual system as well as visual acuity as an important parameter for its assessment. It also deals with achromatopsia as an example of eye disease, the effects of glare on visual performance in daily routine and current clinical or ophthalmological methods of testing visual parameters.

1.1 Visible light

Light plays a very important role in the daily vision process. It is produced by various sources in daily life, e.g. the sun. At the physical level, light consists of electromagnetic radiation, which occurs as an energy wave (Sliney, 2016). The main parameters used to describe a wave are its amplitude, the distance between the wave's maximum and minimum, and its frequency, the number of such waves per second. The wavelength is calculated from the distance between two energy maxima or minima. Light consists of different wavelengths - short, medium and long (Ditchburn, 2013). Visible light is defined as the fraction of electromagnetic radiation that can be perceived by the eye. This proportion falls in a wavelength range from about 400 to 700 nm (Ogherohwo et al., 2015). The perception of brightness does not scale linearly with luminance intensity. It is influenced by the context in which the light is perceived, such as surrounding luminance and spatial context (Bertalmío, 2019; Corney et al., 2009; Purves et al., 2004), but especially by the wavelength of the light. The higher the frequency and the amplitude or the shorter the wavelength, the more energy the light has (Fan et al., 2022). The perception of color is achieved by spectral composition of light (Ogherohwo et al., 2015). Light is called “warm” if it has a long wavelength and less energy (e.g. red light). A light with a short wavelength and high energy (e.g. blue light) is defined as “cold” (Shahidi et al., 2021). Daylight (sunlight) is composed of all

wavelengths. It therefore appears as white (Hernández-Andrés et al., 2001; Ogherohwo et al., 2015). However, with less blue light in the morning or evening, the spectrum is dependent on the time of day and the season (Thorne et al., 2009).

The electromagnetic radiation of light moves in a straight line with so-called light rays (Langley et al., 1997). On their way, light rays can hit different objects, which depending on their structure can lead to different interactions. When the light rays are reflected on a mirroring surface, it is called a reflection. If the energy of the light rays is transferred to the surface, it is called absorption. If light rays pass into another medium, e.g. from air to an aqueous medium, the light refracts (Lüders & Pohl, 2018; Vandergriff & McLean, 2008). Refraction in the human eye is an example of this (Atchison & Thibos, 2016; Gross et al., 2008), providing the starting point for visual perception.

1.2 The eye and the processing of light

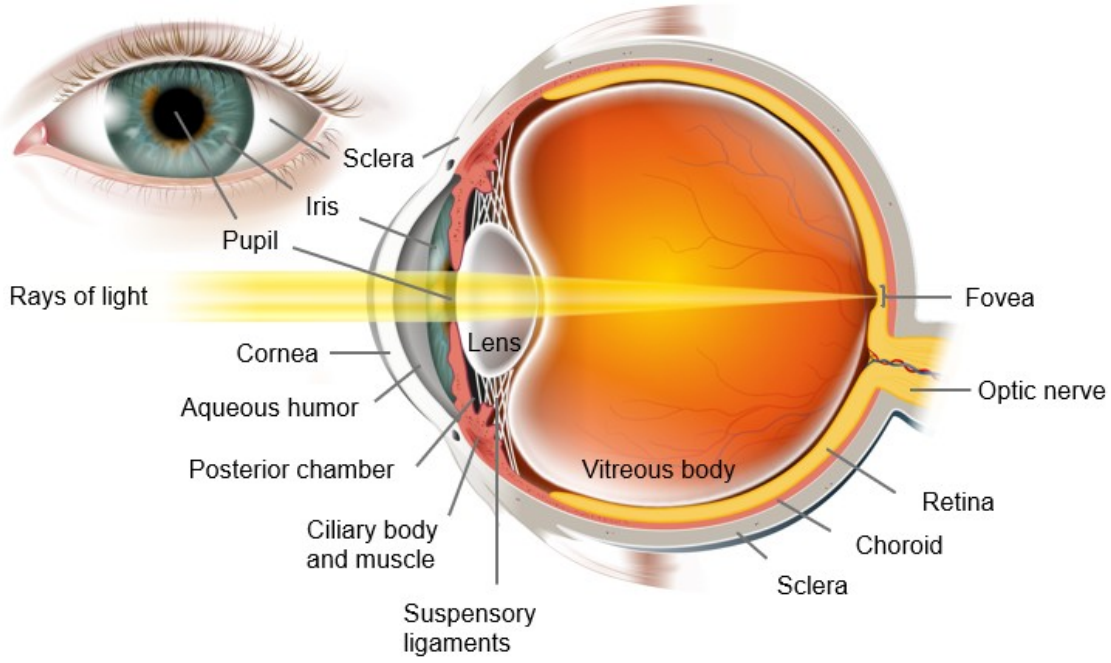

Figure 1 *Schematic structure of a human eye (lateral view). After entering the eye, the light rays pass through various layers of the eye until they reach the retina (Fovea). [Artwork by Irina Stingl]*

„Das Auge macht das Bild, nicht die Kamera.“ - Gisèle Freund

In enabling the brain to form an image of the environment, the eye converts light into nerve impulses, which are then transmitted via the optic nerve to the visual cortex (Rydberg, 1959). The eye can adapt to different levels of brightness. This process of adaptation is possible across a broad spectrum of luminance levels (Ohba & Alpern, 1972). The pupillary light reflex regulates how much light enters the eye (Hall & Chilcott, 2018; Mathôt, 2018) (Figure 1). Light rays entering the eye must pass through the cornea, a transparent layer that covers the pupil and other parts of the eye, where they are refracted (Sridhar, 2018). They then hit the lens behind it, which is attached to so-called ciliary muscles with rigid fibers (zonular fibers). The refractive properties of the lens can be altered by contraction of the ciliary muscles and subsequent relaxation of the zonular fibers, resulting in a curved lens (Guyton & Hall, 2011). In this way, the eye can adjust to “near” or “far”. This process is called accommodation (Atchison, 1995; Glasser, 2006). After passing through the transparent, gel-like vitreous body, which does not contribute to refraction, the light rays hit the retina at the back of the eye, where it covers the inside of the eyeball (Grossniklaus et al., 2015). There is a small pit in the center of the retina, called the fovea centralis, where the light finally hits the retina in a punctiform way (Provis et al., 2013). This is also known as the point of sharpest vision because it contains only cone photoreceptors (Figure 2A) responsible for day and color vision (photopic vision) (Lamb, 2016). A well-functioning refraction and sufficient bundling of the light rays in the fovea centralis is therefore crucial for a sharp image. In a functioning or healthy human eye, there are three types of cones that react differently to certain wavelengths of visible light (short-, middle-, long-wavelength sensitive = S-, M-, L-cones; Figure 2B) (Stockman & Sharpe, 2000). In the periphery of the retina, on the other hand, there are mainly rod photoreceptors (Figure 2A), which require less light and enable us to see at dusk and at night (scotopic vision) (Feigenspan, 2017; Pirenne, 1962; Provis et al., 2013). The light stimulus triggers a photochemical process that leads to a change in potential at the receptor membrane (Lamb, 2022). This change in membrane potential is transmitted via the bipolar cells and ganglion cells in the retina, where the first action potentials are generated. These are then transmitted via the optic nerve to the visual cortex in the brain, where they are processed together with the information from the other eye and assembled into a consciously perceived image (De Moraes, 2013).

Recently, a third light receptor in the retina, the intrinsically photosensitive retinal ganglion cell (ipRGC), was discovered. With a density of 1-2% of the total photoreceptors, these cells represent only a small proportion and have a much slower response time (Kinder et al., 2022). They are particularly sensitive to blue light with a wavelength of around 490 nm, which signals them to suppress the sleep hormone melatonin. Intact IpRGCs are therefore the basis for maintaining the circadian rhythm (Kinder et al., 2022; Pickard & Sollars, 2011; Wong et al., 2005).

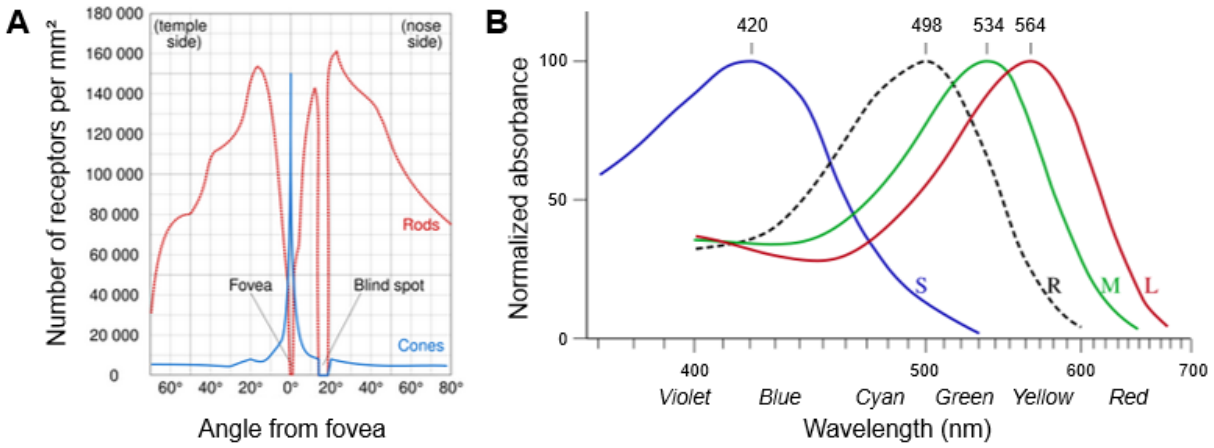

Figure 2 *Rod and cone photoreceptors in the human retina. A) Density of rods (red line) and cones (blue line) in the fovea centralis (only cones) and periphery of the retina (mainly rods with highest density about 20 degrees peripheral to fovea). In the blind spot (exit from the optic nerve) there are no photoreceptors ["Human photoreceptor distribution" by Cmglee is licensed under CC BY-SA 3.0.]; B) Normalized absorbance of cones (S-, M-, L-cones) and rods (R) depending on the wavelength of the visible spectrum ["Cone-absorbance-en" by Vectorized version of the GFDL image Cone-response.png uploaded by User:Maxim Razin based on work by User:DrBob and User:Zeimusu. is licensed under CC BY-SA 3.0.]*

1.3 Visual acuity

Visual acuity represents the visual resolution, i.e. the general ability of the visual system to perceive two neighboring points as separate and thus recognize smallest details (Kniestedt & Stamper, 2003; Wesemann et al., 2020). The theoretical resolution of the retina is defined by the density of cone receptors in the fovea centralis (Hirsch & Curcio, 1989). The quality of the optical image is determined by various external factors as well as the refractive media of the eye and the corresponding correct refraction.

There are different units for reporting visual acuity. Decimal visual acuity is calculated from the reciprocal value of the minimum distance between two points in angular minutes that the eye can still resolve (Bach & Kommerell, 2008). For Landolt rings as optotypes, see next chapter, this is equal to the gap width (in angular minutes) of the smallest recognized Landolt ring (Bach & Kommerell, 2008; Wesemann et al., 2020). The Snellen fraction describes the ratio of the test distance (numerator) to the normal distance (denominator), i.e. the distance at which the size of the optotype corresponds to a decimal visual acuity of 1.0. LogMAR (MAR = Minimum Angle of Resolution) visual acuity is calculated from the logarithm of the gap width (in angular minutes) of the smallest detected Landolt ring (decimal value) (Wesemann et al., 2020). The better the visual acuity, the lower the logMAR value (Bach & Kommerell, 2008). The logMAR values are well suited for statistical calculations and allow the average of different visual acuities to be recorded (Bach & Kommerell, 2008; Westheimer, 1979).

Visual acuity should be scaled logarithmically in order to reflect the level of sensation. For example, if a patient improves from 0.1 to 0.2 decimal, he or she can see just as well at twice the distance (0.2/0.1 = improvement by a factor of 2). However, if a patient with already high visual acuity improves from 1.0 to 1.1 decimal, this increase of 0.1 is almost insignificant (1.1/1.0 = improvement by a factor of 1.1) (Bach & Kommerell, 2008).

The visual angle is defined as the angle at which an object is perceived, meaning the angle between virtual lines from the boundary points of an object to the eye (Bailey & Lovie-Kitchin, 2013). Therefore, the visual angle depends on the size of an object and the viewing distance.

For people with normal vision, this value is at least one angular minute, i.e. 1.0 decimal (Bach & Kommerell, 2008, Bailey 2016). This means that an optotype of 5.82 mm can be detected from 4 meters. In the case of a Landolt ring a gap of 1.16 mm could be resolved. However, younger people very often have an even higher visual acuity value (Ohlsson & Villarreal, 2005). With increasing age, the lens becomes more rigid, loses elasticity and is less able to curve or accommodate resulting in deterioration of visual acuity. This is referred to age-related farsightedness or presbyopia (Atchison, 1995).

The ciliary muscle also becomes weaker, which impairs near vision but not far vision (Glasser, 2006; Strenk et al., 2005).

Visual acuity is the most important parameter for determining visual performance in visual physiology and clinical practice. It is also the most common endpoint in studies (Beck et al., 2007; Schmetterer et al., 2023). A distinction is made between uncorrected (s.c.; lat.: *sine correctione*) and corrected (c.c.; lat.: *cum correctione*) visual acuity, using glasses or contact lenses (Atchison et al., 1979; Guo et al., 2020).

1.4 Methods for determining visual acuity

The international standard DIN EN ISO 8596 and the national standard DIN 58220 are valid for the determination of visual acuity (Dietze, 2018; Wesemann et al., 2020). The approved standard optotype for assessment of visual acuity is the Landolt ring with eight orientations (eight alternative forced choice (8 AFC)) (Bach & Kommerell, 2008; Bailey & Lovie-Kitchin, 2013; Dietze, 2018; Ricci et al., 1998; Rohrschneider et al., 2019; Wesemann et al., 2020). The forced choice method requires the respondent to give an answer, i.e. to guess if necessary (Bach & Kommerell, 2008; Wesemann et al., 2020). The person must indicate the opening direction of the rings shown. This is usually done verbally but is also possible in digitalized form by pressing the corresponding direction on a keyboard (Bach, 1996; Wesemann, 2002). The gap in the ring is 1/5 of the total size (Wesemann et al., 2020). The luminance of the test field (projector, LCD screens, incident light panels) should be between 80-320 cd/m² (Dietze, 2018; Wesemann et al., 2020). The optotype must be at least 80% in contrast. If visual acuity is good, a test distance of four meters is specified; if visual acuity is less than 0.2 decimal, the distance is reduced - usually to one meter. However, ETDRS boards with letters as optotypes (Figure 3) are often used in international studies (Salabati et al., 2024). These are translucent backlit visual test charts (Kaiser, 2009; Shamir et al., 2016). If the 60% criterion has been achieved here, i.e. for example three out of five letters of a row or size have been recognized, this visual acuity level is considered to have been approved (Wesemann et al., 2020). All methods are subjective examination methods that rely on the cooperation of the person being examined.

1.5 Automatic computer-based analysis of visual acuity

It is possible to use computerized tests to examine visual acuity (Bach, 1996; Bailey & Lovie-Kitchin, 2013; Moke et al., 2001; Wesemann et al., 2020). However, the test procedure must comply with the DIN EN ISO 8596 standard. One example is the so-called Freiburger Visual Acuity Test (Bach, 1996), which uses Landolt rings as optotypes. The visual acuity is calculated by using a staircase, called “Best-PEST”-algorithm (Lieberman & Pentland, 1982). The participant gives the answer by pressing the appropriate key on a keyboard symbolizing one of the eight directions of the ring's opening. If the answer is correct, the Landolt ring gets smaller until the opening of the ring cannot be seen anymore. In general, a correct answer will reduce the size of the ring, while a wrong answer will increase it. Depending on the answer, at some point the size of the ring will fluctuate around the threshold (Bach, 1996; Bach & Kommerell, 2008; Wesemann et al., 2020).

1.6 Assessment of mesopic vision and contrast sensitivity

In addition to visual acuity, mesopic vision and glare sensitivity are important parameters for assessing night driving ability or diagnosing congenital stationary night blindness (Aulhorn & Harms, 1970; Van Rijn et al., 2005). The corresponding testing device is called mesoptometer (Aulhorn & Harms, 1965). It presents Landolt rings that remain constant in size but whose contrast is reduced in several steps until the contrast threshold is reached, meaning the contrast value at which the participants can just detect the optotypes. The Landolt ring is offered in a size that is clearly visible and corresponds, for example, to a decimal visual acuity of about 0.1. Thus, the critical parameter is the luminance difference between the optotype and the background. The measurement is done without and with glare on the left side (Bach et al., 2008). Further, contrast sensitivity can be measured by using the so-called Pelli-Robson chart (Figure 3) (Elliott et al., 1990; Mäntyjärvi & Laitinen, 2001). In its horizontal lines there are capital letters that do not get smaller per line, but the contrast of these optotypes decreases. Three optotypes are presented per contrast level here (Pelli, 1988).

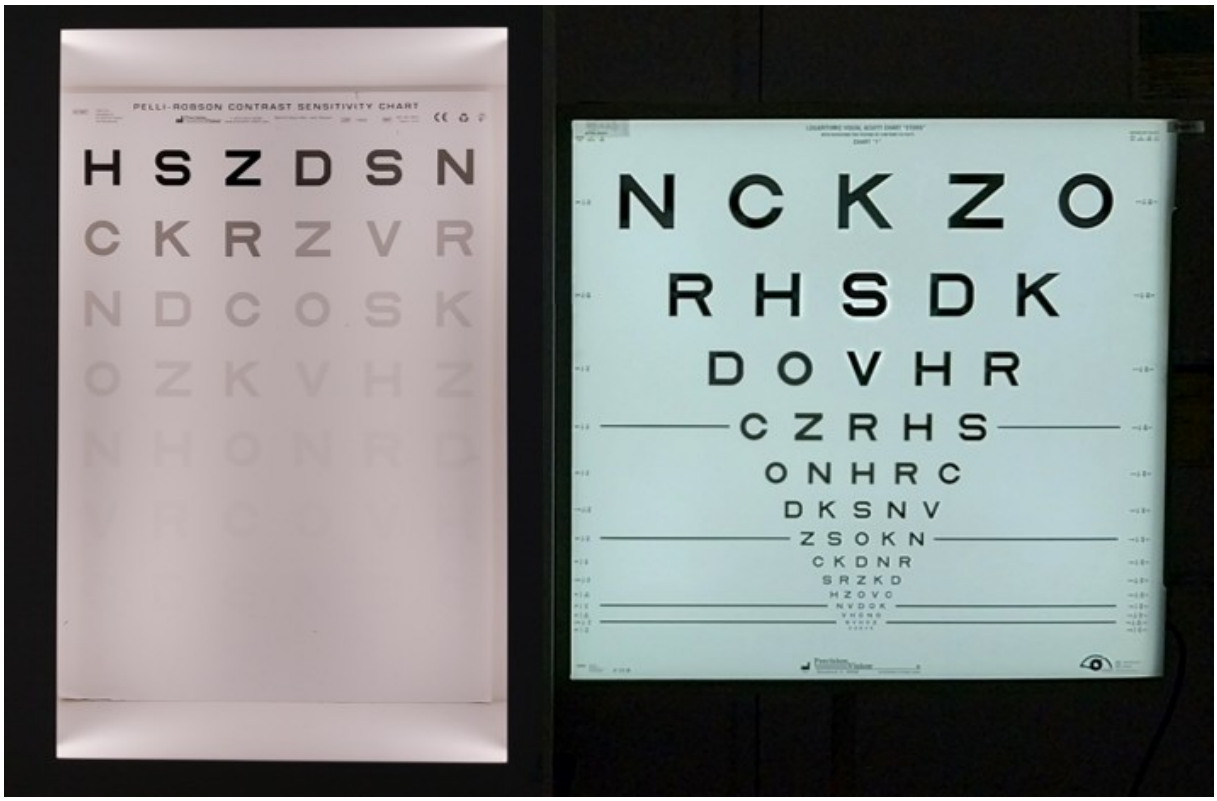

Figure 3 *Vision charts in a darkened room. Left: Pelli-Robson chart for assessing contrast sensitivity; Right: ETDRS chart for measuring visual acuity. [Photographed by Julian Hilmers]*

Contrast is the relative brightness of two surfaces, calculated from the ratio of their different brightness values (Bach et al., 2008). There are five definitions of contrast, all of which can be converted into each other (Bach et al., 2011, 2017). In ophthalmological assessment, the Weber and Michelson contrasts are the most commonly used:

(1) $$\text{Michelson contrast} = \frac{\text{Lmax} - \text{Lmin}}{\text{Lmax} + \text{Lmin}}$$

(2) $$\text{Weber contrast} = \frac{\text{Lmax} - \text{Lmin}}{\text{Lmax}}$$

*with Lmax = maximum luminance, Lmin = minimum luminance

While Michelson contrast is used mainly for grid patterns or realistic images, Weber contrast is used when small objects, such as optotypes, are displayed in front of a large background (Bach et al., 2017).

1.7 Glare and daily luminance

Glare from certain light sources, such as the sun, is a common problem in daily life. Glare is defined as a visual condition that is perceived as unpleasant and leads to a reduction in visual function (Mainster & Turner, 2012; Wolf, 1960). This is caused by too much luminance, or differences in luminance (Mainster & Turner, 2012).

The luminance describes the outgoing luminous flux (Lennie et al., 1993). It is defined as the luminous intensity per area with the unit candela per square meter (cd/m²) (Benedetto et al., 2014). The luminance flux of a light source is therefore particularly high when the luminous intensity is large or the luminous area is small.

$$\text{Luminance} = \frac{\text{Luminous intensity I (cd)}}{\text{Area A (m}^2\text{)}} \tag{3}$$

In everyday life, we are confronted with a wide range of luminances, already reaching 4500 cd/m² on cloudy days (Blankenbach et al., 2010) and 25000 cd/m² or more on sunny days (Cremers & Marx, 2017). Various examples of everyday targets also show values ranging from 30 cd/m² (text on a computer screen) to 8000 cd/m² (Caucasian facial skin in sunlight) to 19000 cd/m² (white road sign in sunlight) (Hilmers et al., 2022).

Another measure is the illuminance, which indicates the incident luminous flux per surface of an object (Michael et al., 2020). It is measured in lux (lx), which is equal to one lumen per square meter (lm/m²) (Benedetto et al., 2014). Regarding the eye, the illuminance thus describes how much light enters the eye through the pupil.

$$\text{Illuminance} = \frac{\text{Luminous flux f (lm)}}{\text{Area A (m}^2\text{)}} \tag{4}$$

The CIE (International Commission on Illumination) defines two types of glare, physiological and psychological glare (Englisch, 2017). While psychological glare (discomfort glare) is described as a condition where vision is not noticeably impaired, but the glare is only perceived as unpleasant, physiological glare (disability glare) is a condition that can lead to a reduction in visual performance without necessarily causing

discomfort (Englisch, 2017; Hartmann, 1963). Physiological glare is a measurable quantity, whereas psychological glare describes the subjective perception of the observer and is therefore individual.

1.8 Achromatopsia as an example of an eye disease with photophobia

Functional cones are an important part of the eye for processing everyday light conditions (Stockman et al., 2006). However, some people have non-functional cones. Achromatopsia, for example, is an autosomal recessive retinal disease that results in non-functioning cones (Remmer et al., 2015). This is usually caused by mutations in the *CNGA3* or *CNGB3* gene (Baxter & Borchert, 2024; Fischer et al., 2020; Johnson et al., 2004; Kohl et al., 2005; Li et al., 2014). The loss of cone function leads to typical symptoms: reduced visual acuity, sensitivity to glare (photophobia), nystagmus and complete color blindness (Johnson et al., 2004; Remmer et al., 2015). Achromats can therefore only perceive contrasts (light-dark) (Kohl et al., 2005; Remmer et al., 2015). While there is currently no effective treatment, gene therapies are being researched (Baxter & Borchert, 2024; Fischer et al., 2020; Reichel et al., 2021). Preliminary good safety and efficacy have been shown in some studies (Baxter & Borchert, 2024). Promising results in activating dormant cone signaling pathways have been achieved using gene therapy in the early stages of visual development (Farahbakhsh et al., 2022). While the total loss of color perception seems to be the most severe limitation for people with normal vision, patients with achromatopsia suffer most from the enormous sensitivity to glare, which is the most limiting factor in their daily lives. To reduce this photophobia, many of these patients use sunglasses, filter glasses, or tinted contact lenses that block short-wavelength light in the visible spectrum that cause glare (Andersen et al., 2024; Hilmers et al., 2023; W. L. Park & Sunness, 2004; Rohrschneider & Bach, 2018; Severinsky et al., 2016).

2 Motivation and objectives

As early as the mid-19th century, there were historically important steps in the testing of eye function. It was the German ophthalmologist Kuechler, for example, who reported on the need for standardized eye tests (Colenbrander, 2001). At the end of the century, Donders described the concept of visual acuity, for which Snellen later developed an optotype as a unit of measure (Colenbrander, 2001; de Jong, 2024). The test procedure and units of measurement continued to evolve throughout the 20th century. From today's perspective, visual acuity testing has long been an integral part of ophthalmological examinations and serves as an important endpoint, particularly in ophthalmological studies (Beck et al., 2007; Schmetterer et al., 2023). Standards for visual acuity testing have been defined and adapted over time. Presently, visual acuity should be tested between a luminance of 80-320 cd/m² and a contrast of at least 80% (Dietze, 2018; Wesemann et al., 2020). However, these are laboratory conditions that reflect only a small part of the constantly changing luminance and contrast in everyday life. Especially in sunshine, but also on cloudy days, luminance levels are much higher (Blankenbach et al., 2010; Cremers & Marx, 2017). Even for people with healthy eyes, it is therefore difficult to draw conclusions about everyday vision with the standard condition. Patients with photophobia are much more affected by light (Ochsner & Zrenner, 1992). This includes patients with the eye disease achromatopsia. Photophobic patients with achromatopsia have reported to us that they often perform better in visual acuity tests than their subjective perception in natural scene really is, and that they are much more impaired than their visual acuity as measured by standardized tests would suggest. As soon as they left the building and went outside, they were extremely dazzled by the lack of cone function and their vision, or subjectively perceived visual acuity, was enormously reduced. In addition, in a gene therapy trial in Tübingen, Germany (EudraCT No: 2014-001874-32), achromatopsia patients subjectively reported an improvement in glare sensitivity in everyday life after treatment. However, there was no test that could adequately assess this and at the same time provide information on daily visual performance. The aim of this work was therefore to develop an automated visual acuity test that would reflect visual acuity under everyday conditions, i.e. determining visual acuity threshold at different luminances and contrasts. This visual acuity test was to be validated for its repeatability and for the visual performance of people with normal vision and those with glare

sensitivity - achromatopsia patients. It was expected that the visual performance of people with photophobia would decrease significantly with increasing luminance and decreasing contrast. Moreover, a new score was to be developed that describes the visual acuity space by combining the three parameters of visual acuity, luminance and contrast. The score is intended to aid in the rapid assessment of a therapeutic approach. The effect of corrective lenses to prevent photophobia, in this case edge filter glasses, also needed to be evaluated in order to be used as evidence for patients to obtain reimbursement from their health insurance companies.

3 Major findings

The following section briefly summarizes the major key findings of the three studies, which are detailed in the papers or manuscripts in the appendix (study I - III).

3.1 New vision test that quantifies the dynamics of visual acuity as a function of luminance and contrast in a unified visual acuity space

The automated VA-CAL test (**V**isual **A**cuity at different levels of **C**ontrast and **A**mbient **L**uminance) proved to be a suitable device for the simultaneous assessment of visual acuity at different contrast and luminance combinations common in daily living situations. It provides a more comprehensive assessment of spatial vision in everyday life presented as three-dimensional ‘visual acuity space’ (Hilmers et al., 2022, Figure 3 in study I). Participants with normal vision showed good test-retest variability with an overall intraclass correlation of 0.63. The three parameters visual acuity, luminance and contrast cover a visual acuity space in which the dynamics of visual acuity in relation to luminance and contrast can be easily evaluated (Hilmers et al., 2022; see study I).

3.2 Visual performance of eye-healthy people and problems of patients with photophobia remain partially undetected in the standard acuity assessment according to DIN EN ISO 8596

People with healthy eyes improved their visual acuity up to an ambient luminance of 3000 cd/m² to a maximum mean visual acuity of -0.47 logMAR (+- 0.03 SEM; at

contrast = 95%), a luminance range far above the defined standard condition of 80-320 cd/m² (DIN EN ISO 8596). At luminance levels tested above 3000-5000 cd/m², visual acuity deteriorated. A reduction in contrast also led to a deterioration in visual acuity at all luminances. This suggests that people with healthy eyes may have better visual acuity at certain luminance levels (1000 cd/m², 3000 cd/m², 5000 cd/m²) typical of everyday situations, which is not detected by standard tests (Hilmers et al., 2022, Figure 3 in study I).

Using the VA-CAL test, the photophobia of the achromatopsia patients was reflected in their visual performance. Their visual acuity deteriorated continuously from 30 cd/m² (mean +- SEM: 0.76 +- 0.046 logMAR, contrast = 89%) up to a luminance of 10000 cd/m^2 (mean +- SEM: 1.41 +- 0.08 logMAR, contrast = 18%), which means a difference in visual acuity by a total of 0.6 logMAR (Hilmers et al., 2023, Figure 2 in study II). A deviation of more than two lines (0.2 logMAR) reliably indicates a clinically relevant change in visual acuity (Petersen, 1993; Rosser et al., 2003). Reducing contrast also tended to worsen visual acuity. Since the standard visual acuity test is performed at 80-100 cd/m², the visual acuity of achromatopsia patients under everyday life conditions is most likely overestimated, not detecting this severe visual impairment due to high luminance and low contrast (Hilmers et al., 2023; see study II).

3.3 Edge filter glasses as an aid for people who are sensitive to glare

In everyday life, achromats often use so-called edge filter glasses, which filter out short-wave light and thus reduce glare. However, patients have problems getting these filters reimbursed by their health insurance. So far, there is no clinically standardized way of expressing the degree of disability of a person affected by glare in numerical terms. Even people with healthy eyes use them to improve contrast or as a blue light filter. The effect of edge filter glasses on visual acuity has been studied using VA-CAL. While the use of an edge filter glass (550 nm) in people with normal vision resulted in a 0.1 logMAR deterioration in visual acuity in all conditions (Hilmers et al., 2023, Figure 2A/B + Figure 4A in study II), an improvement in visual acuity was achieved in achromats in almost all luminance-contrast combinations tested, with a visual acuity improvement of up to 0.23 logMAR, particularly at high luminances (Hilmers et al., 2023, Figure 2C/D + Figure 4B in study II). The study results prove that edge filter

glasses help to improve visual acuity of achromatopsia patients and people with photophobia in everyday life situations. Furthermore, the results underline the usefulness of edge filter glasses in this patient population and provide arguments for the assumption of costs by the health insurance (Hilmers et al., 2023; see study II).

3.4 Score for assessment of visual performance

To generate a score for clinical application that describes visual performance as a function of luminance and contrast, subregions were created within the visual acuity space that contain certain testing points and thus visual acuity values for certain luminance-contrast combinations (Hilmers et al., 2023, Figure 4 in study II). The so-called VA-CAL score is calculated from the mean visual acuity values achieved at three neighboring testing points. To determine the effect of treatments such as filter glasses, logMAR differences were calculated between each visual acuity measurement before and after treatment, or without and with a filter (Hilmers et al., 2023, Figure 4 in study II). Corresponding color coding is used to quickly assess the result, with green indicating an improvement in visual acuity, red indicating a deterioration in visual acuity and grey indicating a constant visual acuity (Hilmers et al., 2023; see study II).

3.5 Effects from glare of different light sources on visual acuity and glare perception

The effect of uniform and point light sources on the visual acuity of people with normal vision under everyday contrast and illuminance conditions, and their subjective perception of glare, was also investigated. The mean difference in visual acuity between the uniform light source and four point light sources at 23.5° eccentricity (near-peripheral) was statistically significant for people with normal vision, showing better visual performance with near-peripheral point light (Hilmers et al., 2025, Figure 2 + Table 2 in study III). Illuminance and contrast also had a statistically significant effect on visual acuity for all glare types (Hilmers et al., 2025, Table 1 in study III). There was a statistically significant difference in the discomfort score only for the illuminance level and not for the type of glare (Hilmers et al., 2025, Table 3 in study III). In general, the uniform light source was judged to be the least dazzling (Hilmers et al., 2025, Figure 3 in study III). Glare from peripheral point sources appeared to have less effect on visual

acuity in healthy eyes than glare from paracentral point sources (13.3° eccentricity) or uniform glare (Hilmers et al., 2025; see study III).

4 Discussion

The following section explains the background to the results and discusses the advantages and disadvantages of the VA-CAL test. It also proposes improvements as well as future developments and research.

4.1 Visual acuity space reflecting everyday life

While standard visual acuity measurements are done with a maximum optotype contrast and a luminance level lying between 80-320 cd/m² (Wesemann et al., 2020), the VA-CAL test covers a large proportion of the conditions that occur in everyday life (Hilmers et al., 2022). In particular, contrasts from 18% to 95% and luminances from 0 to 10000 cd/m² are examined. Own luminance measurements on everyday targets (e.g. white road/information sign with 19000 cd/m²) in sunshine have shown that even higher luminances prevail, which are not even observed by VA-CAL (Hilmers et al., 2022, page 8 in study I). Other researchers have reported daily luminance examples ranging from 4500 cd/m² on cloudy days (Blankenbach et al., 2010) to 25000 cd/m² on sunny days (Cremers & Marx, 2017). It can therefore be assumed that the visual acuity of glare-sensitive patients in everyday life is even worse than that described with VA-CAL for luminance conditions of 1000-10000 cd/m² (Hilmers et al., 2023, Figure 2 + Table, page 4 ff. in study II), and that even people with healthy eyes will eventually fall into moderately impaired visual performance due to glare in daily life.

For photobiological safety reasons, a luminance of 10000 cd/m² was not exceeded in VA-CAL (Hilmers et al., 2022, 2023). Higher luminance levels can lead to increased risk to the eye and absolute glare, resulting in protective responses such as squinting, head and eye movements (Empfehlung der Strahlenschutzkommission, 2006). Therefore, according to the lamp safety standard, the exposure limit for a source emitting in the visible spectral range is not exceeded (Udovičić et al., 2013). Because of the limits described, it can thus be excluded that there is a risk of eye damage even at the maximum luminance of 10000 cd/m² used.

In everyday life, we are often confronted with scenes in which contrast and luminance conditions change rapidly (Hayasaka et al., 2022; Mante et al., 2005). The eye therefore needs to adapt quickly to these different conditions. Although it would be possible to measure visual acuity outdoors, it would always depend on the weather, the seasons or the time of day. Outdoors it would therefore be difficult to create comparable conditions between two measurements, so no reliable results could be obtained or comparisons made. For studies, opticians or in everyday clinical practice, though, it is important to have comparable conditions that have led to the use of a single condition at low light level in clinical practice. VA-CAL provides reliable visual acuity results over a broad range of everyday contrast and luminance values. However, the VA-CAL test uses white light. Fluctuations in daylight and possible differences in color temperature sensitivity are therefore not taken into account by VA-CAL, nor are equiluminant chromatic conditions or recognition via movement. An additional measure would be to use warm light, which occurs in the morning and evening hours. It can be assumed that people are less glare sensitive to warm light because it contains less blue light, which is mainly responsible for glare.

4.2 Comparison to commercial vision tests

Conventional measurement methods, such as the ETDRS vision chart (Shamir et al., 2016), do not include the different luminance levels of everyday life. In addition, visual acuity, contrast sensitivity and glare sensitivity are often tested separately. To the best of our knowledge, there is no automated test that evaluates visual acuity under everyday conditions, i.e. that determines the visual acuity space (extending between the luminance and contrast axes) (Hilmers et al., 2022, 2023).

Contrast sensitivity is measured using Pelli-Robson charts (Pelli, 1988). The size of the letters used as optotypes remains the same, only the contrast changes. After three letters with the same contrast, the next triplet with the next lower contrast is presented (Elliott et al., 1990; Mäntyjärvi & Laitinen, 2001). In contrast to VA-CAL, visual acuity is therefore not considered in the Pelli-Robson test. In addition, this test is only performed at a single low level of brightness. Grating stimuli are also often used to test contrast sensitivity, in which light and dark bars of varying width (spatial frequencies) and contrast are presented alternately per stimulus, and the subject must indicate the

direction in which they are presented (Kelly, 1977). The changing light conditions of everyday life are not taken into account here either.

Commercial glare tests typically use point light sources. However, these are less relevant for most daily activities in daylight. Point light sources are particularly relevant at night, for example when driving in the dark (Jones et al., 2022). In contrast, a large uniform luminance background, such as that used in VA-CAL, provides a good representation of everyday situations in daylight. However, there was only a small difference in visual acuity between peripheral point light sources and uniform light sources in normal-sighted people (Hilmers et al., 2025, Figure 2 + Table 2, page 7 in study III). To reflect living conditions with different conditions of lighting, both light sources would have to be used to determine daily visual performance.

Previous studies have already confirmed the negative effect of point light sources on visual performance (Kimlin et al., 2017; Wood, 2020). This was also shown in our research (Hilmers et al., 2025). But, as point sources were subjectively perceived as more unpleasant, a greater effect on visual acuity might have been expected, in contrast to uniform glare. Visual performance would certainly have been even more impaired with a smaller glare angle, e.g. 0.25° to the glare source (Jones et al., 2022), than more peripheral point light sources used here (13.3° and 23.5°; Hilmers et al., 2025, page 3 in study III). It cannot be excluded that disease related glare-sensitivity, such as in achromatopsia or cataracts, would have led to a more severe impairment of visual performance due to point light sources. This is particularly likely in the case of cataracts, where the halo effect and light scattering occurs (Babizhayev et al., 2009). It may be worthwhile investigating the relation between such disorders and the effect of various types of glare light sources in the future.

Visual discomfort is the subjective impairment of viewing certain stimuli, with blurred vision often reported (O'Hare & Hibbard, 2013). Blurred vision is thought to be associated with a decline in visual performance or visual acuity. Therefore, the VA-CAL results (Hilmers et al., 2022, page 6 ff.; Hilmers et al., 2023, page 4 ff.; Hilmers et al., 2025, page 6 ff.) could be interpreted in such a way that good visual acuity or its improvement means increasing visual comfort, whereas a deterioration in visual acuity means visual discomfort. However, it is recommended that both objective and

subjective measures are taken to determine visual discomfort (Lambooij et al., 2007). The Ocular Photosensitivity Analyzer (OPA), a device that quantifies the visual photosensitivity threshold, is a test that allows such an assessment of discomfort (Verriotto et al., 2017). The mean monocular visual photosensitivity threshold of 35 healthy subjects was found to be approximately 800 lux, slightly lower when repeated (Verriotto et al., 2017). This device reaches even higher levels of brightness (32000 lux) than VA-CAL does. However, the outcome is only a subjective assessment and there is no hard parameter such as visual acuity. In general, VA-CAL in the future could incorporate a rating that describes the discomfort of each luminance level. The rating should be done in the presence of the various luminance levels rather than retrospectively, e.g. by the examiner explicitly asking and recording it on a worksheet during the trial, or by pressing an appropriate number on the numeric keypad. The assessment could be made using an extended version of de Boer's scale (Gellatly & Weintraub, 1990) from 0 to 10, where 0 is no discomfort and 10 is maximum discomfort to pain, as used in the glare source comparison study (Hilmers et al., 2025, Figure 3, page 8 in study III).

The room in which the VA-CAL test is performed can be relatively small, as the test is done from a distance of one meter (Hilmers et al., 2022, 2023). In principle, the test could be performed also for greater distances, such as 4 meters. Own measurements with a lux meter have shown that the illumination at eye level is reduced from about 4000 lux at one meter to about 400 lux at four meters. At greater distances, the luminous intensity of the light would have to be increased to result in comparable effects.

4.3 Explanation of the participants' visual behavior

In Hilmers et al. (2022, page 8 ff. in study I) we have lined out that the visual acuity of people with normal vision is underestimated in the standard condition. Participants with healthy eyes reached their maximum visual acuity (approximately one line better than in the standard condition) when the ambient luminance was increased to 3000-5000 cd/m². This is due to the function properties of the cones, the photoreceptors in the human retina responsible for photopic vision (Provis et al., 2013). Luminance levels higher than the standard condition between 80-320 cd/m² appear to

be the better luminance conditions for optimal visual acuity, as also reported by others (Hauser et al., 1992). Accordingly, especially at low contrasts with luminances above 5000 cd/m², there is a deterioration in visual acuity due to stray light, which reduces retinal contrast and contrast sensitivity. At even higher luminances, rhodopsin is also bleached, reducing visual performance (Alpern, 1971). As expected, visual acuity generally deteriorates with decreasing contrast because the visual system is less able to distinguish the optotypes from the background (Elliott & Bullimore, 1993).

Our research mainly included young participants with normal vision (Hilmers et al., 2022, 2023). However, it is not yet known whether this increase in visual acuity under such optimal lighting would also occur in an older population. As the pupil size decreases with age, the ability to respond to changing light conditions is reduced (Telek et al., 2018; Winn et al., 1994). This effect would be particularly relevant regarding the low luminance conditions used in VA-CAL. At brighter light, however, no difference would be expected. It is also expected that the narrower pupil at brighter light compensates to some extent for the lack of accommodation, as there is a greater depth of focus due to the pinhole effect (Kanclerz et al., 2024; Onyszkiewicz et al., 2024). Cataracts development increases with age (Asbell et al., 2005). The opacity of the lens affects the refraction of light, resulting in increased light scattering (Fujikado et al., 2004). As a result, light rays from optotypes or images do not reach the fovea centralis with its high cone density properly, or cannot be processed, making the eye more sensitive to glare. A similar effect occurs in dry eye disease, which is often caused by reduced tear production in older age, leading to increased light scattering on the uneven surface of the eye and thus increased sensitivity to glare (de Paiva, 2017). Therefore, an older population may not benefit from increased luminance in terms of visual acuity.

The visual acuity of patients with achromatopsia in daily living tasks is often overestimated under the dim standardized ambient luminance condition (80-320 cd/m²) in a clinical testing room (Hilmers et al., 2023, page 8 ff. in study II). Achromats have only rods, which are responsible for scotopic vision (Barbur & Stockman, 2010; Kohl et al., 2005; Remmer et al., 2015). In healthy eyes, the center of the fovea centralis contains only cones and no rods (Lamb, 2016). Achromats therefore have no functioning photoreceptors in the center of the retina (Blackwell &

Blackwell, 1961), while the representation of the fovea in the visual cortex is very large (Azzopardi & Cowey, 1993). Their pure rod vision thus leads to lower visual acuity (Johnson et al., 2004). Rods are sensitive to luminances between 10^{-6} and 10 cd/m², whereas cones are activated by luminances ranging from about 0.03 to 10^{8} cd/m² (Ferwerda et al., 1996). When glare or increased luminance is added, the rods become oversaturated excessively and cannot function anymore for coding contrasts (Aguilar & Stiles, 1954). The result is a loss of spatial vision and a further decline in visual performance (Hilmers et al., 2023). Although achromats can achieve decimal visual acuities of 0.2 in standard clinical settings, they reach visual acuity levels of legal blindness (decimal VA < 0.02) at outdoor conditions room (Hilmers et al., 2023, Figure 2, page 4 in study II). Finally, achromats suffer from nystagmus, which often worsens with increasing luminance, making it even more difficult to focus on fine details such as optotypes.

The maximum sensitivity of rods lies in the short wavelengths of the visible light spectrum, resulting in a higher sensitivity to light with a high blue content (Kraft et al., 1993). Cut-off (or edge) filters are therefore particularly suitable for photosensitive individuals such as achromats (Rohrschneider & Bach, 2018), which is further highlighted by the results of our research (Hilmers et al., 2023, Figure 4, page 7 in study II). Edge filters cut off the short-wavelength part of the light sources (e.g. < 550 nm), meaning blocking it. This reduces the glare effect of the short-wavelength light and improves contrast vision (Schornack et al., 2007). Our results showed an improvement of more than two lines of visual acuity with filter glasses, even at high ambient luminance, clearly demonstrating their usefulness for achromatopsia patients (Hilmers et al., 2023, Figure 2, page 4 in study II).

Moreover, we showed that people with normal vision do not benefit from edge filters, as we did not find any improvement in visual acuity. Instead, they experienced a deterioration in visual acuity when using them in all luminance-contrast conditions (Hilmers et al., 2023, Figure 2, page 4 in study II). This can be explained by the filter-related reduction in retinal illumination (Hilmers et al., 2023).

Achromats have also reported working unconsciously with afterimages at high luminance levels. These are images seen immediately after the intense light

stimulating the eye has ceased, for example when closing the eyes (Phillips, 2013). The unnatural prolonged fixation on the grey or black Landolt ring optotype with the same stimulus intensity led to Rhodopsin bleaching related fatigue of the photoreceptors (Alpern, 1971). When they closed their eyes for a moment, the previous Landolt ring appeared in white as an afterimage and they decided the possible gap direction based on this. However, it is not possible to prove which of the two conditions they were using for their decision and to what extent this led to correct or incorrect answers. Especially since achromats showed poor visual performance at higher luminances and it seems that the use of afterimages did not help either.

4.4 VA-CAL score as an endpoint

For new treatment options, such as gene therapy for achromatopsia (Fischer et al., 2020), there is always a need for clinical endpoints that extend the standard BCVA. In particular, subjective effects (reduced glare sensitivity) have been reported by participating patients, which could not be measured objectively by previous endpoints. Based on the most commonly used standardized endpoint for vision, visual acuity (Beck et al., 2007; Schmetterer et al., 2023), we developed the new VA-CAL score to provide a unified description of visual acuity space that overcomes the limitations of the standard BCVA with just a single condition. The score is calculated using either the mean value of three absolute visual acuities of neighboring testing points (combination of contrast and ambient luminance) in the visual acuity space or using the differences between baseline and post-intervention, respectively (Hilmers et al., 2023, Figure 4, page 7 in study II). A similar calculation is used in the contrast sensitivity function to calculate the area under the log contrast sensitivity function (AULCSF) (Shandiz et al., 2011), although only one value is output, which includes all spatial frequencies, and it is not clear at which spatial frequency a change in contrast sensitivity occurs due to a treatment or the like. For example, if the VA-CAL score is used to monitor the success of a treatment such as after gene therapy, it becomes clear in which region of the visual acuity space a treatment related change occurs. This may be particularly relevant for a patient who is sensitive to glare, as it occurs at high luminance levels not regularly assessed. The color coding of the VA-CAL score (green = VA improvement; red = VA deterioration; grey = same VA; Hilmers et al., 2023, Figure 4, page 7 in study II) aims to make the test results quick and easy to understand and is inspired by the

presentation of results from other tests such as microperimetry (Macula Integrity Assessment (MAIA) decibel color scale; Macular Integrity Index) (Rohrschneider et al., 2008).

VA-CAL was already employed as a clinical endpoint in one of the first gene therapies in ophthalmology, the CNGA3IIb study for the treatment of achromatopsia (EudraCT No: 2014-001874-32), which is currently undergoing final evaluation. However, to further demonstrate its usefulness as an endpoint for specific conditions, VA-CAL and the use of the score should be implemented in further clinical trials. Once the score is used as an endpoint in a clinical trial and the results of that clinical trial influence the management of a specific condition, such as achromatopsia, there should be sufficient clinical relevance to warrant further consideration. A visual acuity difference of 0.3 logMAR is considered necessary by the Food and Drug Administration (FDA) to prove clinical relevance. With a VA-CAL score difference of about 0.2 logMAR the considered 0.3 logMAR difference was not achieved by using an edge filter in achromatopsia (Hilmers et al., 2023). Nonetheless, considering the logarithmic progression of visual acuity, an improvement just below this threshold for patients with low visual acuity is enormous and of high clinical relevance. Moreover, a visual acuity improvement of 0.2 logMAR is sufficient for a statistically significant change (Petersen, 1993; Rosser et al., 2003).

4.5 Modifications and improvements of the current setup

Using VA-CAL, we were able to confirm the dependence of visual acuity on ambient luminance and contrast in patients with achromatopsia and demonstrate the beneficial effect of edge-filter lenses at high luminances for these patients (Hilmers et al., 2023, page 4 ff. in study II). But it is still unclear whether they would benefit in a comparable way from neutral density filters, which only reduce luminance but do not provide spectral filtering (i.e., like sunglasses). The issue of grey filters is becoming increasingly relevant and has already been addressed by other scientists (Andersen et al., 2024). The growing use of these filters has also been reported to us by the board of the German Achromatopsie Selbsthilfe e.V.. A grey filter reduces the number of photons by the same factor at all wavelengths, whereas a chromatic cut-off filter only blocks light up to a certain wavelength. Therefore, for comparability, a grey

filter must be used that has the same scotopic efficiency as the edge filter in achromats. If neutral density had a comparable benefit, grey filters would be a cheaper alternative to edge filters, resulting in lower costs for patients. Personal feedback from achromatopsia patients shows individual preferences for edge filters or grey filters. It could be hypothesized that filter preference depends on the spectrum of incident light. Therefore, further research is needed to investigate how different color temperatures (midday vs. evening or indoor vs. outdoor) affect visual performance with the different filters by applying so-called Kelvin correction filters to modify the color temperature, e.g. from 6000 K to 3000 K.

The current implementation of the VA-CAL test is rather time-consuming (about 1.5 hours) due to the number of luminance-contrast combinations tested. In addition, the prototype used in the previous studies uses a projector for presenting the optotypes, rendering the complete setup rather large and requires a specially prepared room. Both of these issues could be a problem in everyday clinical practice. We have therefore reduced the setup to a smaller, more mobile version, using four commercially available LED panels to create uniform glare and a tablet computer in the center to present the optotypes. Additionally, it is mounted on a movable stand. To reduce the time required for defining the visual acuity space, the number of test points (combinations of ambient luminance and contrast) was reduced to a minimum based on our previous data. This 'short version' measures acuity at only 17 contrast-luminance combinations, reducing the time required for a test to about 25 minutes. The maximum luminance is 5000 cd/m², a level of light that allows pathology to be detected, can still be performed by patients who are sensitive to glare, and at the same time represents the luminance of everyday life, which can lead to glare effects. In a recent study (ID: DRKS00028003 in the German Clinical Trials Register) we investigated whether comparable results could be reliably obtained using this short version. Moreover, the visual performance of three groups of patients was examined: Ten patients with cataract, ten patients with cone dystrophy and 24 patients with achromatopsia. For comparison, 68 participants with normal vision were additionally measured. In addition, a subgroup of 46 patients were tested twice on different days for test-retest reliability and 24 achromats were tested three times (test-retest and 1-year follow-up). The results of the study are currently being analyzed and will be published.

Although the short version of the VA-CAL test reduces time enormously and is well suited for clinical trials, it should be further reduced for use in busy daily clinical practice when administered by a clinician. The VA-CAL score requires at least eight measurements for building corresponding subregions (Hilmers et al., 2023, Figure 4, page 7 in study II) (three luminances; three contrasts at the lowest and highest luminance, two contrasts at the medium luminance; triangle formation = eight areas of interest). In this case, a measurement time of approximately eleven minutes - one minute for the assessment of each visual acuity value and one minute for the adaptation to each luminance value - cannot be exceeded. However, many tests in ophthalmology, such as visual field testing or electrophysiology, take 10-30 minutes or even longer (e.g. dark adaptation). As everything is automated, the patients could be placed in front of the device and perform the test themselves, without supervision, if necessary, but with initial instructions. Conventional tests, such as the ETDRS chart, give specific decimal visual acuity values, e.g. 1.0, 1.25, 1.6 and 2.0 decimal in the upper visual acuity range (Shamir et al., 2016). The VA-CAL test currently identifies values in between, e.g. 1.44 decimal, in a refined search, which could be advantageous for the accurate assessment of various everyday situations and a finer assessment of the success of a therapy. However, the algorithm could be adapted to make the threshold even faster by widening the limits.

Only four measurements would be required if VA-CAL was used at a low light level and 5000 cd/m² luminance. Two contrasts could be presented per light level because of the linear contrast dependence (Hilmers et al., 2022, Figure 3C, page 5 in study I). Since reference values for people with normal vision and glare-sensitive patients with achromatopsia are known (Hilmers et al., 2022, 2023), the assessment and any conclusions about a possible pathology would focus on the reference values corresponding to the visual acuities obtained. It would also be possible to assess whether there is a shift towards the values of healthy people after appropriate treatment of the patients. In this slimmed-down version, however, the VA-CAL score with the subregions would be neglected, which could lead to the loss of important information about corresponding regions in the visual acuity space. Nevertheless, in clinical trials it would depend on the functional target of the treatment which version of the VA-CAL test should be employed.

Another alternative calculation to obtain a time reduced assessment of visual performance could be to determine the best individual visual acuity at a particular luminance and contrast. The first step would be to identify the best luminance at maximum contrast, i.e. the luminance at which visual acuity is best. This could be done by initially setting the Landolt ring rather small and performing a short, quick test without ambient luminance to determine baseline visual acuity. With this ring size fixed, the light would then be increased slowly and gradually. The direction of opening of the rings had to be correctly indicated three out of five times per gradient. Otherwise, this luminance would be set as the limit. Once the highest possible luminance has been found, the same would be done with a reduction in contrast. The threshold and the end of the test could be one line of visual loss. Ultimately, the best individual visual acuity would be achieved in two-dimensional space under the most difficult conditions. The higher the luminance and the lower the contrast, the better the visual performance. An improvement in glare perception and contrast vision would be achieved if the best acuity was reached with higher luminance and/or lower contrast than before.

4.6 Further research topics

The VA-CAL test has also been used to investigate the effects of pinhole occlusion and pilocarpine on visual acuity at different contrasts and ambient luminances in presbyopes as well as emmetropes, and to make recommendations about the potential and limitations of pharmacologically induced miosis as a treatment for presbyopia based on the results (Onyszkiewicz et al., 2024). Pupil narrowing is known to improve near vision (Hughes & Neer, 1981). The pinhole effect associated with pupil constriction increases the depth of field by limiting the distorted rays of light entering the eye (Kanclerz et al., 2024; Onyszkiewicz et al., 2024). Special pinhole lenses are often used to achieve this pinhole effect and improve near vision in presbyopes (H. H. Park et al., 2019). Onyszkiewicz and colleagues used pharmacological treatment with commercially available pilocarpine eye drops, which also causes pupil constriction (Rosenfield, 2022). Pilocarpine was found to have no effect on visual acuity in presbyopes and could therefore be a useful alternative to spectacles in everyday life (Onyszkiewicz et al., 2024).

To assess the minimum detectable color contrasts and the effect of glare on them, VA-CAL was adapted by Strasser and team using specific colored Landolt rings on a colored background (Strasser et al., 2025). They tested people with normal color vision as well as people with color vision deficiency, and all groups showed increased color contrast thresholds due to higher glare levels. The results and exact procedure will be presented at the Association for Research in Vision and Ophthalmology meeting in 2025. With this adaptation, the VA-CAL test could also be used to study color vision and use that as an endpoint in therapies, such as gene therapy for achromats.

We have previously shown that glare from peripheral point sources has less effect on visual acuity in healthy eyes than glare from paracentral point sources or uniform glare (Hilmers et al., 2025, page 6 ff. in study III). In another experiment, a sheet of simulated raindrops could be used to create a diffuse light distribution instead of a sheet of frosted glass through which the background light passes uniformly (Hilmers et al., 2022, Figure 1, page 2 in study I). This would simulate driving a car in the rain during the day and the respective view through a windscreen. It can be expected that this would also reduce the visual performance of young people with normal vision compared to a uniform light distribution (Konstantopoulos et al., 2010). In addition, a comparison can be made between young and older people to test visual performance during the day in the rain, particularly in relation to fitness to drive.

4.7 Suitability for patients of clinical practice

VA-CAL proved to be suitable for assessing the dependence of visual acuity to ambient luminance and contrast in patients with achromatopsia and in younger people with normal vision (Hilmers et al., 2022, 2023). Patients with cataracts or cone dystrophies also show an increased sensitivity to glare and therefore often have problems with changing light conditions in everyday life. It remains to be seen whether VA-CAL would be suitable for this group of patients and whether it would result in disease-specific visual acuity characteristics. However, cataract surgery is very common in clinical practice (Davis, 2016; Tabin et al., 2008). The benefits of surgery could be demonstrated for different types of intraocular lenses by comparing visual performance before and after surgery. Even for people with astigmatism (Read et al., 2007), which also distorts light, VA-CAL may provide a more accurate representation of their visual

performance in everyday life. Older people in the achromatic group who took part in our studies did not report having problems with pressing the buttons on the keypad or making many accidental errors. So, it seems to be feasible for older people, which means that using VA-CAL can also provide information about visual performance in everyday life in advanced age.

Experience from the short version study (DRKS no. DRKS00028003) has shown that the test is in principle also suitable for children. We recommend that it be used from the age of six, or as soon as they can independently use the keyboard to locate the appropriate directions. Focusing on ETDRS charts, researchers have described reliable and comparable results as soon as children can recognize letters (Manny et al., 2003). Others have looked at the differences between the most commonly used vision tests in children, the LEA test and the ETDRS charts (Dobson et al., 2009). The result of their study is that the LEA test gives a better result than the ETDRS charts (Dobson et al., 2009). In VA-CAL, the optotypes could be changed from Landolt rings to LEA visual signs when testing children, although it should be noted that these are copyrighted. In general, LEA signs would represent more typical objects or shapes from everyday life and provide a stronger link to everyday life. It would also be possible to use a 4AFC procedure for children or to give the information verbally. The recording should then be done by an independent person.

5 Conclusion

The aim of this doctoral thesis was to investigate how the visual acuity of people with normal vision and patients with achromatopsia behave with ambient luminance levels and contrasts of everyday life. Therefore, a new test, the VA-CAL test, was developed to assess visual acuity at luminances up to 10000 cd/m² and contrasts between 18% and 95%. The standardized normal condition defined in DIN EN ISO 8596 for testing visual acuity, with a fixed luminance value between 80-320 cd/m² and maximum contrast, examines only one luminance-contrast condition in the visual acuity space and therefore does not allow conclusions to be drawn about visual behavior under all other everyday conditions, as VA-CAL does. As hypothesized, the automated VA-CAL test showed that the visual acuity of people with normal vision and glare-sensitive patients with achromatopsia was different under luminance-contrast conditions that deviated from the norm. Both worsened their acuity when the optotype contrast was reduced. People with normal vision improved their visual acuity with luminance levels above the norm reaching their maximum visual acuity at luminances of 3000-5000 cd/m². Measuring under standard conditions therefore underestimates the true visual acuity of people with normal vision. In contrast, the visual acuity of glare-sensitive achromats deteriorated with increasing luminance to the point of severe visual impairment. This severe impairment, e.g. on sunny days, remains undetected by a standard measurement, which therefore overestimates the visual acuity of glare-sensitive patients. The results of VA-CAL can therefore be used to provide patients with a real representation of their visual performance and can be considered, for example, when categorizing the degree of disability. Edge filter glasses, which block shortwave light, are often used by these patients to reduce glare. We found that wearing these glasses was an appropriate aid for glare-sensitive patients, as it improved their visual acuity by more than two lines, particularly at high luminance levels, preventing severe visual impairment. VA-CAL can thus serve as important evidence to help these patients with health insurance reimbursement and could be further used to investigate other aids, such as neutral density filters. In addition, the work presented here described a new score that represents visual performance as a function of luminance and contrast, assessing the average visual acuity of specific subregions within the visual acuity space.

Nevertheless, VA-CAL also has its limitations. For example, the uniform light output reflects daytime conditions in particular. For night-time driving, point light sources should also be used for testing. In addition, the current version is a time-consuming test that requires a specially prepared test room. Therefore, a mobile version with a shorter test program has been developed for clinical use, which only includes certain luminance-contrast combinations based on previous results, thus reducing the testing time. In this short version, VA-CAL is intended to become established in everyday clinical practice, enabling patients and staff to draw new conclusions. Further adaptations, such as the use of different optotypes, are possible and should be investigated in the future.

The VA-CAL test showed good repeatability in people with normal vision. It was easy to perform in this population and in patients with achromatopsia. However, to become established in everyday clinical practice, further studies with other patients and age groups should be done to verify the feasibility and their visual behavior in the visual acuity space.

Overall, the combination of visual acuity and contrast vision in changing everyday ambient luminances is novel. To our knowledge, there is no single automated visual acuity test that captures the dynamics of continuously changing visual acuity under different ambient luminances and contrasts. In the future, this will provide new insights into the everyday visual performance of different groups of people. A new score that describes different levels of acuity within the visual space has never been developed before. The VA-CAL score provides an overview of visual performance under everyday luminance and contrast conditions and offers the opportunity to validate potential therapeutic success as an endpoint and a unified measure of vision.

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List of publications appended

Accepted publications

I. Hilmers, J., Straßer, T., Bach, M., Stingl, K., & Zrenner, E. (2022). Quantification of the Dynamic Visual Acuity Space at Real-World Luminances and Contrasts: The VA-CAL Test. *Translational Vision Science & Technology*, *11*(4), 12-12. DOI: 10.1167/tvst.11.4.12

II. Hilmers, J., Bach, M., Stingl, K., Zrenner, E., & Straßer, T. (2023). The VA-CAL Test Quantifies Improvement of Visual Acuity in Achromatopsia by Means of Short-Wave Cutoff Filter Glasses in Daily Living Conditions. *Translational Vision Science & Technology*, *12*(6), 20-20. DOI: 10.1167/tvst.12.6.20

Manuscripts in preparation (preprint)

III. Hilmers, J., Koschka, M., Zrenner, E., & Straßer, T. (2025). The Impact of Glare Type and Intensity on Objective and Subjective Visual Performance. *MedRxiv*. DOI: 10.1101/2025.04.18.25326064

Statement of contributions

Study I: Quantification of the Dynamic Visual Acuity Space at Real-World Luminances and Contrasts: The VA-CAL Test.

Hilmers, J., Straßer, T., Bach, M., Stingl, K., & Zrenner, E. (2022). Quantification of the dynamic visual acuity space at real-world luminances and contrasts: the VA-CAL test. *Translational Vision Science & Technology*, *11*(4), 12.

EZ indicated the high relevance of the topic. The implementation, setup and study protocol were discussed and designed collectively by JH, EZ and TS. The setup was constructed by JH with the help of the clinic's internal workshop. JH and TS developed the software for the visual acuity test. JH performed the measurements with the participants. KS took care of the preliminary medical examinations. EZ and TS supervised the project. JH and TS analyzed the data. JH wrote the manuscript and prepared the graphs included. All authors critically discussed the results and contributed to the final manuscript by proofreading and adjustments.

Study II: The VA-CAL Test Quantifies Improvement of Visual Acuity in Achromatopsia by Means of Short-Wave Cutoff Filter Glasses in Daily Living Conditions.

Hilmers, J., Bach, M., Stingl, K., Zrenner, E., & Straßer, T. (2023). The VA-CAL test quantifies improvement of visual acuity in achromatopsia by means of short-wave cutoff filter glasses in daily living conditions. *Translational Vision Science & Technology*, *12*(6), 20.

The setup and study protocol were discussed and designed collectively by JH, EZ and TS. The setup was constructed by JH with the help of the clinic's internal workshop. JH and TS developed the software for the visual acuity test. JH performed the measurements with the participants. KS took care of the preliminary medical examinations. EZ and TS supervised the project. JH and TS analyzed the data. JH wrote the manuscript and prepared the graphs included with suggestions of EZ and TS. All authors discussed the results and contributed to the final manuscript by proofreading and adjustments.

Study III: The Impact of Glare Type and Intensity on Objective and Subjective Visual Performance.

Hilmers, J., Koschka, M., Zrenner, E., & Straßer, T. (2025). The Impact of Glare Type and Intensity on Objective and Subjective Visual Performance. *MedRxiv.*

The setup and study protocol were discussed and designed collectively by JH, EZ and TS. The setup was constructed by JH and MK. JH and MK performed the measurements with the participants. EZ and TS supervised the project. JH and TS analyzed the data. JH wrote the manuscript with the help of TS. All authors discussed the results and contributed to the final manuscript by proofreading and adjustments.

Publications

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Article

Quantification of the Dynamic Visual Acuity Space at Real-World Luminances and Contrasts: The VA-CAL Test

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Purpose: Best-corrected visual acuity (BCVA) is assessed at a single standardized luminance with maximum optotype contrast, not reflecting the constantly changing daily-life viewing conditions. For a more realistic estimation of visual performance at varying object contrasts (Cs) and ambient luminances (ALs), we developed a new VA test, VA-CAL.

Methods: Landolt-C-rings between 18% and 95% Weber contrast, were presented at 1 m distance (8 Alternative Forced Choice) on a 5.7 degree field in the middle of a frosted glass screen (66 degrees), back-lit by 3060 LEDs (generating ambient luminances between 0–10,000 cd/m^2). Visual acuity (VA) was measured in 14 normally sighted participants twice for 8 conditions of ambient luminance and 6 conditions of contrast using a QUEST staircase procedure.

Results: VA improved continuously up to an ambient luminance of 3000 to 5000 cd/m^2 (best mean VA $\pm$ SEM: -0.47 ± 0.03 logMAR at C = 95%, AL = 3000 cd/m^2), followed by a decline of VA at higher luminances with good test-retest variability. As expected, reduced contrast leads to a lower VA (worst mean VA $\pm$ SEM: -0.03 ± 0.03 logMAR at C = 18%, AL = 0 cd/m^2). A 3D plot of these data shows the VA space (VAS) extending between the contrast and luminance axes, which describes the dynamics of VA continuously changing under varying everyday life conditions.

Conclusions: VA-CAL, an automated device and procedure, allows for simultaneous evaluation of VA at various contrast-luminance combinations, thus providing a more comprehensive assessment of spatial vision problems not seen with standard BCVA tests.

Translational Relevance: The new BCVA test VA-CAL incorporates a range of everyday contrast and ambient luminance conditions for a more realistic description of visual performance.

Introduction

Visual acuity (VA) tests serve as the most important parameter for assessing visual performance in clinical examinations. Currently, clinical VA measurement is based on standards, such as DIN EN ISO 8596, and is performed at a specific ambient luminance (AL) of between 80 and 320 cd/m^2 (recommended = 200 cd/m^2) with maximum optotype contrast.[1] This condition does not necessarily represent daily outdoor environments, where the AL reaches 2000 to 8000 cd/m^2 even on cloudy days[2] and therefore significantly exceeds the defined luminance range of the clinical VA test. Visual perception deals constantly with quickly changing object contrast and variation of AL under which such objects are viewed. Thus, standardized VA testing does not necessarily reflect the actual visual performance in daily life, including outdoor situations, which are especially difficult to master for patients

with inherited retinal disorders with increased glare-sensitivity like achromatopsia.[3,4] Healthy participants can show an increase in VA up to a luminance of 5000 cd/m^2.[5] Many methods aim to determine VA (e.g. Early Treatment Diabetic Retinopathy Study [ETDRS],[6] the Bailey-Lovie chart,[7] or the Freiburg Visual Acuity and Contrast Test [FrACT]).[8] Glare sensitivity at changing AL is determined with separate devices, like the commonly used mesoptometer, the Ocular Photosensitivity Analyzer,[9] or the Brightness Acuity Tester.[10] Other tests determine contrast sensitivity, like the Pelli Robson chart,[11,12] or the quick contrast sensitivity function method (qCSF),[13] as well as FrACT.[8] However, to the best of our knowledge, there is no automated single test for assessing the visual acuity space (VAS; extending between luminance and contrast axes), which describes the dynamics of VA continuously changing under varying everyday life conditions.

Here, we present a new VA test, VA-CAL, which allows to determine these dynamics of VA depending on the actually viewed objects' contrast under varying everyday luminance conditions, thus detecting abnormalities of spatial vision that go unnoticed in clinical best-corrected visual acuity (BCVA) tests.

Materials and Methods

Participants

VA-CAL was tested in 14 eye-healthy participants (7 women and 7 men) aged between 21 and 29 years (mean ± SD = 25.2 ± 2.8 years) at the Institute for Ophthalmic Research Tuebingen. All of them underwent a second measurement about 6 weeks later. The duration of the test was about 3 hours. BCVA (ETDRS chart), slit-lamp examination, and optical coherence tomography (OCT) was performed in an initial ophthalmic examination at the first visit. The inclusion criteria were a monocular BCVA of 0.1 logMAR or better and no suspected or confirmed eye disease.

Before testing, participants were informed about the aims and purpose of the study, and they gave their written consent to study participation. The protocol was approved by the Institutional Review Board of the medical faculty of the University of Tuebingen (431/2019BO2) and followed the Declaration of Helsinki.

Experimental Design

The VA-CAL setup, depicted in Figure 1, is characterized by a 130 cm × 130 cm (66 degree edge length) semitransparent frosted glass screen, which can be back-lit with luminances of between 0 and 10,000 cd/m^2 using an array of computer-controlled (via DMX RGB(W) Controller 8356; Solarox Holding GmbH, Dessau-Roßlau, Germany) high-power LEDs (Power Flat LED Tapes, 6000K; Solarox Holding GmbH), mounted on a metal plate at a distance of 26 cm. According to the lamp safety standard, a radiation source emitting in the visible spectral range with a luminance of up to 10,000 cd/m^2 does not exceed the exposure limit and poses no danger to the observer.[14] The optotypes are presented in the center of the screen on a magnetically fixed light-tight white circular testing surface (10 cm in diameter) using a projector (Notevision Sharp PGA20X; Sharp K.K., Sakai,

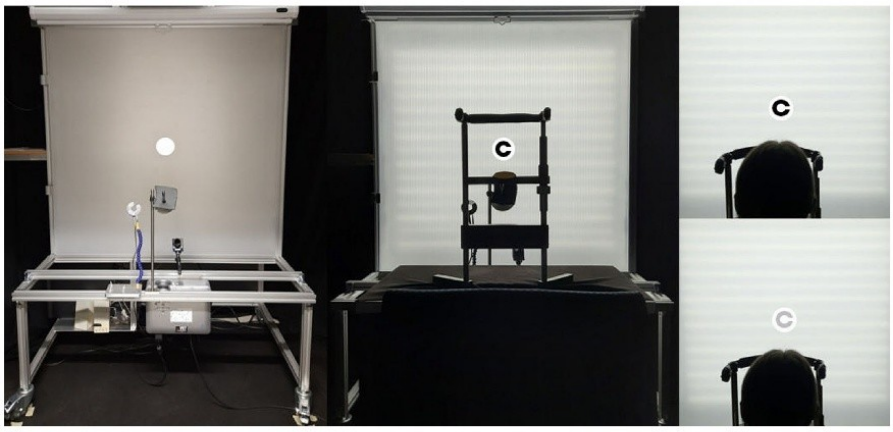

Figure 1. Experimental setup (VA-CAL setup, *center*) backlit by computer-controlled LEDs (*left*) generating different ambient luminances. Landolt C-rings can be presented at different contrasts (*right*). The pictures were modified for better visibility of the projected Landolt C-ring.

Japan), positioned parallel to the frosted glass screen on an aluminum bar, with the optic lens at 58 cm height. The image is presented on a mirror, fixed at 99 cm height with an angle of 76 degrees. The standard optics of the projector were removed and exchanged for a collecting lens (f = 100 mm) so that the conventional image size (81 cm × 61 cm) of the projector fits the size of the central testing surface. Walls, floor, and ceiling are covered with black fabric. A headrest is positioned at 1 m distance and 1.2 m height. For recording pupil diameter, an infrared camera (DMK 21AU04; The Imaging Source GmbH, Bremen, Germany) is positioned in front of the participant. The investigator sits outside the chamber and controls testing procedure via the main computer (Windows 10 Pro, Intel Core i5-4590 CPU).

Procedure

VA-CAL was programmed with PsychoPy (version 3).[15] The VA threshold for each condition was determined by modulating Landolt C-ring (LCR) sizes from largest to smallest diameter using the QUEST adaptive staircase method.[16] This staircase is based on the respondent's responses and continuously alters the size of the optotype according to the threshold.[17] It measures the threshold using a Weibull psychometric function with threshold at 63.2% correct. The QUEST procedure stops either if the width of 5% to 95% confidence interval of the estimated threshold (gap size of the LCR) falls below 0.03 degrees or if the maximum number of 60 trials has been reached. The threshold was normally reached after 15 to 20 trials. The first stimulus was always presented above the expected threshold with a visual angle of the LCR gap size of 0.042 degree (=VA of 0.4 logMAR).

Table 1 lists the AL and corresponding illuminance values used in VA-CAL. In addition, VA was determined at an AL of close to 0 cd/m^2, with LEDs being switched off. The AL was calibrated beforehand with a luminance meter (LS-100; Konica Minolta Holdings K.K., Chiyoda, Japan). The corresponding LED level was directly controlled by PsychoPy. The illuminance at 1 m distance and 1.2 m height, the participant's eye position, was measured with a luxmeter (Voltcraft MS-1500 digital luxmeter; Conrad Electronic SE, Hirschau, Germany). The chromaticity coordinates (x, y, and z) of the background luminance on the CIE diagram were (0.323, 0.330, and 0.347, respectively), similar to CIE standard illuminant D65.[18] Chromaticity was measured with a digital spectrometer (USB4000-UV-VIS-ES; Ocean Optics Inc., Del Ray Beach, FL, USA) at a distance of 1 m.

The testing surface had the same background luminance as the AL generated by LEDs from 320 cd/m^2 to 5000 cd/m^2. Below this range, the luminance of the testing surface was 100 cd/m^2 and above this range, it was limited to 6800 cd/m^2, the maximum luminance of the projector.

The contrast was calibrated for each luminance level by adjusting the gray value of the optotype in

Table 1. Ambient Luminances, Corresponding Illuminance Levels at the Participant's Eye Position at a Testing Distance of 1 m and Suitable Examples of Daily Life From Literature[2] and Own Measurements

Ambient Luminance in VA-CAL	Corresponding Illuminance at 1 m	Examples[2] of Daily Life With Corresponding Luminance	Own Measurements With Luminance Meter
30 cd/m^2	20 lux	White paper under lamp Text on computer screen	Caucasian facial skin (over cheek bone in interior lighting, office)
320 cd/m^2	260 lux	Wall, ceiling (with interior lighting, office) Computer display	White paper under interior lighting (office) Max. BCVA background (DIN EN ISO 8596)
1000 cd/m^2	770 lux	Daytime road surface	White car (in shadow, sunny day)
3000 cd/m^2	2300 lux	Traffic lights Full moon	Doctors' white coat (in shadow, sunny day)
5000 cd/m^2	3700 lux	Overcast sky (daytime)	Surface of cobblestones (in sunlight)
8000 cd/m^2	6200 lux	Blue sky (daytime)	Caucasian facial skin (over cheek bone in sunlight)
10,000 cd/m^2	7800 lux	Wet (reflective) road	White FFP2 face mask (in sunlight) White porcelain plate on table (in sunlight)

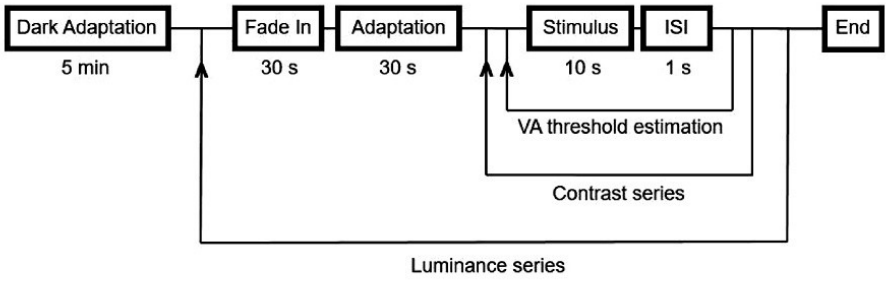

Figure 2. Testing procedure of VA-CAL. After an initial dark adaptation period, the ambient luminance was increased in steps (fade-in) to the next presented luminance level, followed by an adaptation time. Within each ambient luminance, the VA threshold was determined for each contrast using the QUEST adaptive staircase method by adjusting the size of the Landolt C-rings.

PsychoPy so that the luminance of the LCR (L_{min}) and of the testing surface (L_{max}) gave the desired Michelson contrast.[19] For further use and analysis, it was converted into the Weber contrast, best suited for contrast denomination of our particular condition.[19]

In VA-CAL, LCRs were presented in Weber contrasts of 18%, 33%, 46%, 66%, 82%, and 95%. Due to insufficient L_{max} for ALs of 0 cd/m^2 and 30 cd/m^2, the 95% contrast could only be measured from an AL of 320 cd/m^2.

The VA-CAL test was performed monocularly, using the eye with better VA or the dominant eye in cases with equal VA in both eyes, without pupil dilation using refraction of the BCVA of the ETDRS test (no near addition necessary due to young age[20]). The participants' refraction was corrected with the appropriate spherical and cylindrical lenses inserted into a trial frame. The participants had to identify the gap direction of LCR by pressing the corresponding button on a keypad (LogiLink wireless keypad ID0173, 2direct GmbH, Schalksmühle, Germany). The LCR gaps were presented randomly in eight different directions (8 Alternative Forced Choice Method). The participants received auditory feedback if their response was correct (low pitch) or wrong (high pitch). If the gap direction of LCR was not recognizable, they were asked to guess the direction. The participants were instructed to respond as fast as possible within 10 seconds, followed by 1-second interstimulus interval (ISI). No responses were considered as wrong.

Response times of 12 volunteers with normal vision (age = 22–29 years, mean = 25 years) were recorded during the VA measurements with VA-CAL. Response time was defined as the time between the presentation of the optotype and the participants' response by pressing the button on the wireless keypad. Response time measurements were not possible in two participants due to technical problems.

The testing procedure is shown in Figure 2. After 5 minutes dark adaptation, the VA-CAL test started with the lowest AL. Between the presentation of different luminances, there was a fade-in time of 30 seconds in which the luminance was increased in steps until the required level was reached, followed by adaptation time for another 30 seconds (1 min adaptation in AL 0 cd/m^2 and 30 cd/m^2 without fade-in). Subsequently, LCRs were presented at varying contrasts, starting with the highest C (95%) and finishing with the lowest (18%).

A fixation cross subtending 0.23 degrees was displayed in the middle of the testing surface during the entire luminance adaptation phase (fade-in period and adaptation plateau). The contrast value of the cross corresponded to the subsequent first-tested maximum contrast. In addition, the fixation cross was presented during ISI (i.e. between the stimuli), for orientation. During such ISIs, the fixation cross always had the same contrast level as the corresponding contrast series.

Statistical Analysis

All statistical analyses were performed with JMP 15 (SAS Institute, Cary, NC, USA). Mean values and SEM of the logMAR VA were calculated (N = 14, Fig. 3, see Supplementary Table S1 in S1). For testing the normality of the data, we used the Anderson-Darling test. Data of the participants' second visit were used for assessing the test-retest variability (see Supplementary Table S2 in S1).

Luminance and contrast effects on the response time were analyzed with a restricted maximum likelihood method using the participant as random effect, contrast, and luminance as fixed effects. In order to determine the shortest acceptable correct response time, we calculated the 1% level, eliminating outliers due to the "happy trigger effect" (i.e. 99% of all

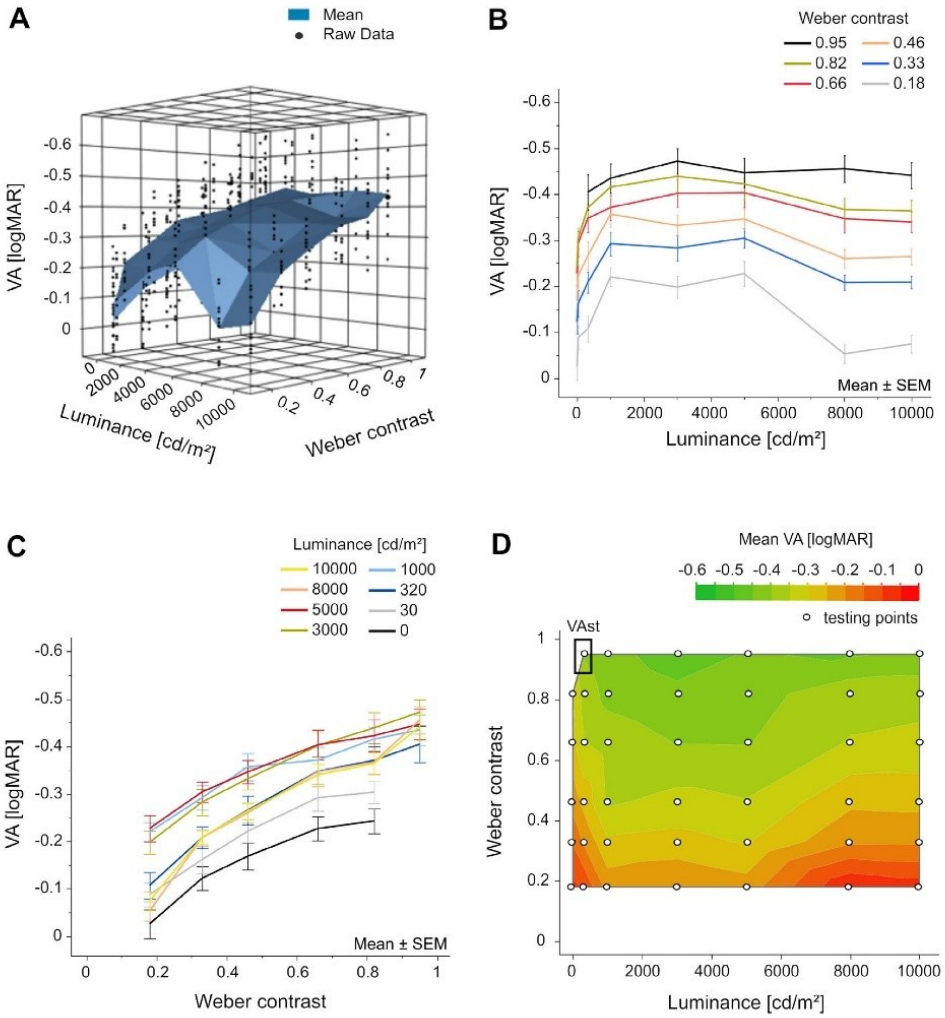

Figure 3. Mean and SEM of the visual acuity threshold of healthy participants for different levels of contrast and ambient luminance. (**A**) Mean values ($N = 14$) are depicted by *blue surface*. *Black dots* symbolize single measurements in each observer. (**B**) Two-dimensional representation with luminance on the abscissa. Different contrasts are represented by different colors. (**C**) Two-dimensional representation with contrast on the abscissa (CS curve). Different luminances are represented by different colors. (**D**) Heat map of averaged VA (logMAR) with Weber contrast and luminance. *Black rectangle* depicts the conditions for standard VA measurement (mean $VA_{st} = -0.41$ logMAR). *White filled circles* show different testing points of VA-CAL.

responses were of longer duration). The last four responses within a test condition were evaluated, ensuring that the response values were close to the VA threshold.

The intraclass correlation coefficient (ICC) for testing the test-retest variability of VA-CAL was calculated according to the formula of Chen et al.[21] by using a linear mixed model, which includes the visit and the participant as random effects, and the contrast and the ambient luminance as well as their interaction as fixed effects. The ICC (2-way random, single measure; ICC[2,1] with agreement definition and 95% confidence interval)[22] for the single testing conditions (C + AL) were determined using IBM SPSS Statistics (version 27). Further, overall paired *t*-test (Bland-Altman-Analysis)[23] was done for checking repeatability of first and second measurement without differentiation between luminance and contrast.

In order to allow for a quick overview of visual performance, VA differences in six different regions of interest (RSI; Table 2) were calculated in relation to the individual maximum VA. Therefore, these VA

Table 2. Region of Interests (RSI) and Corresponding Conditions for Investigation of VA Differences to the Participants' Personal Maximum VA Within These RSI

Region of Interest	Conditions
1 (high contrast, low luminance)	Weber contrasts ≥50% (66%, 82%, and 95%) Luminances 0, 30, and 320 cd/m^2
2 (low contrast, low luminance)	Weber contrasts <50% (18%, 33%, and 46%) Luminances 0, 30, and 320 cd/m^2
3 (high contrast, medium luminance)	Weber contrasts ≥50% (66%, 82%, and 95%) Luminances 320, 1000, and 3000 cd/m^2
4 (low contrast, medium luminance)	Weber contrasts <50% (18%, 33%, and 46%) Luminances 320, 1000, and 3000 cd/m^2
5 (high contrast, high luminance)	Weber contrasts ≥50% (66%, 82%, and 95%) Luminances 3000, 5000, 8000, and 10,000 cd/m^2
6 (low contrast, high luminance)	Weber contrasts <50% (18%, 33%, and 46%) Luminances 3000, 5000, 8000, and 10,000 cd/m^2

differences of each participant at any testing conditions were first calculated and then averaged by the number of participants ($N = 14$; see Supplementary Table S3 in S1). VA differences of the corresponding conditions of each RSI were averaged. A paired-samples *t*-test was conducted to determine a difference between maximum VA (VA_{max}) and the standard BCVA (VA_{st}) achieved at the testing condition comparable to the clinically measured BCVA according to DIN EN ISO 8596 (at AL = 320 cd/m^2, C = 95%).

The pupil diameter ($N = 12$) was analyzed with ImageJ (version 1.8.0)[24] by marking the corresponding area on images taken at the end of the luminance adaptation time and was measured by using a previously determined pixel to millimeter ratio (1 pixel = 0.286 mm). Pupil measurement of two participants was not possible due to technical problems.

Results

The VA measured with the ETDRS chart in each participant ranged from 0 to −0.3 logMAR (mean ± SEM = −0.19 ± 0.03 logMAR). Spherical refractive errors of the participants ranged from + 2.0 to −3.5 diopter, with cylinders of up to −1.75.

In Figure 3A, the mean VA (blue) averaged from the data of 14 participants (black dots, see Supplementary Table S1 in S2) is shown within the 3D space describing VA under different conditions of luminance and contrast as a VAS. Figure 3D depicts this data as a heat map in which mean VA is presented in different colors. Figure 3B and C show the same data but depicted as VA depending on luminance and contrast respectively in 2D presentation. A figure depicting the data on a log-log scale is shown in the supplement (S1); we prefer linear scales in order to better discern abnormalities in the clinically critical higher luminance range. Data were normally distributed ($P = 0.059$). As expected, lowering the contrast leads to a reduction of VA in all participants. The VA declined at AL 320 cd/m^2 with a reduction of contrast from −0.41 logMAR (mean ± 0.04 SEM logMAR; 95% C) to −0.11 logMAR (mean ± 0.03 SEM logMAR; 18% C). Interestingly, the shape of the contrast sensitivity curve was not affected by the different luminance conditions (Fig. 3C), but is only shifted along the VA axis. However, the VA of the participants improved from the lowest AL of 0 cd/m^2 (mean ± SEM = −0.24 ± 0.03 logMAR at C = 82%) over an AL of 320 cd/m^2 (=VA_{st}; mean ± SEM: −0.41 ± 0.03 logMAR at C = 95%) up to its maximum at an AL of 3000 to 5000 cd/m^2 (contrast dependent; best VA mean ± SEM = −0.47 ± 0.03 logMAR at C = 95% and AL = 3000 cd/m^2). With higher ALs up to 10,000 cd/m^2, VA remained relatively stable at 95% contrast. At lower contrasts, VA decreased again up to an AL of 10,000 cd/m^2, near to the VA value reached with AL 320 cd/m^2 (see Fig. 3).

Figure 4 depicts the ICCs of 14 participants for each testing condition. The ICCs ranged from 0.43 (at AL = 30 cd/m^2 and C = 82%) to 0.94 (at AL = 3000 cd/m^2 and C = 95%). Especially at ALs above 1000 cd/m^2 and high contrast, there was very good test-retest variability. Smaller ICCs occurred especially at both low AL and low contrast. In all conditions, a good

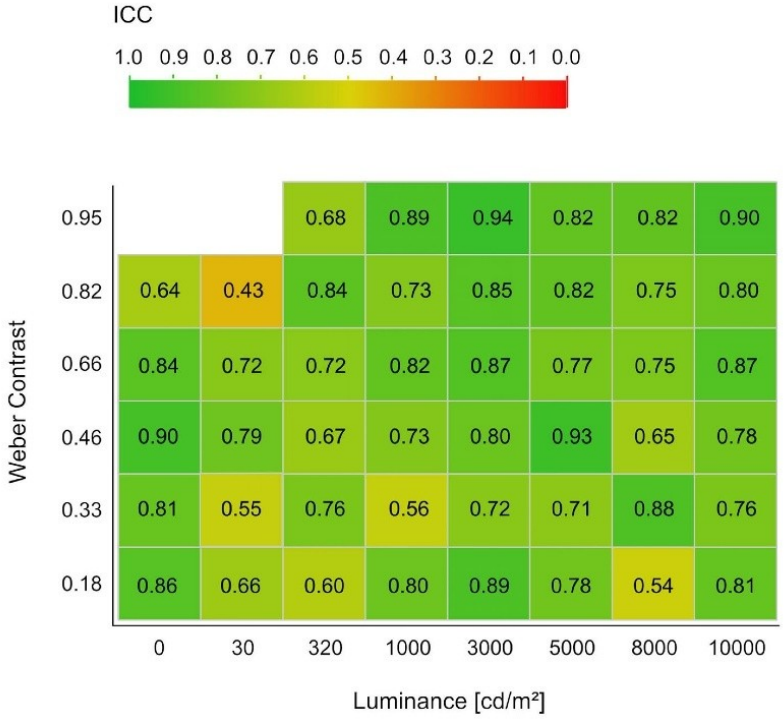

Figure 4. Intraclass correlation (ICC) for each test condition. Colors represent the ICC, ranging from *green* (very good to good repeatability; range = 1.0–0.6), over *yellow* (medium; range = 0.6–0.4) to *red* (ICC <0.4).[25]

or very good ICC was reached. The overall ICC was 0.63, which is considered as good reliability,[25] proving good agreement and repeatability of the VA-CAL test. Paired *t*-test between the first and second measurements resulted in a mean difference of −0.008 logMAR (SD = 0.003, 95% confidence interval [CI] = 0.0024 to −0.0141, $P = 0.0056$, correlation = 0.86).

Figure 5 shows the averaged VA differences to the maximum VA for each RSI (see Table 2 for luminance and contrast conditions). Green indicates no or only a small difference, yellow a moderate difference, and purple a large difference between VA for the respective combination of AL and contrast and the individual maximum VA. Standard BCVA (VA_{st}, white rectangle) denotes the mean VA obtained at the standard condition of our setup (320 cd/m^2 luminance and 95% contrast) comparable to the clinical VA measurement norms (DIN EN ISO 8596; luminance [80–320 cd/m^2] + contrast [>90%]). Overall, participants show the best visual performance at high contrasts, combined with a medium or high luminance (RSI 3 and 5). VA most notably decreased at low luminance levels at both contrast levels (RSI 1), as well as at lower contrasts in all luminance RSIs (RSI 2, 4, and 6). VA_{st} and VA_{max} are illustrated by white rectangles. The VA_{max} (mean ± SEM = −0.50 ± 0.03 logMAR) was reached at an AL of between 320 and 10,000 cd/m^2 (median = 4000 cd/m^2; Q(25) = 3000 cd/m^2, Q(75) = 8500 cd/m^2). Mean VA_{max} exceeds VA_{st} (mean ± SEM = −0.41 ± 0.04 logMAR) of −0.09 logMAR. There was a statistically significant difference between VA_{max} and VA_{st} ($t(13) = 5.40$, $P = 0.0001$).

The 1% level for the shortest acceptable response time (eliminating outliers) was 611 ms for correct responses. The response time was highly significantly increased by lower contrast ($P < 0.0001$), but not by luminance ($P = 0.048$). Near the threshold, correct responses ($n = 1161$; mean ± SEM = 1.71 seconds ± 0.02) were increased in average compared to overall response time ($n = 6118$; mean ± SEM = 1.51 seconds ± 0.01).

Unsurprisingly, the initial pupil diameter at AL 0 cd/m^2 (mean ± SEM = 5.61 ± 0.34 mm) decreased with increasing luminance before remaining stable at about 3000 cd/m^2 (mean ± SEM = 2.57 ± 0.07 mm; see Supplementary Fig. S2 in S1).

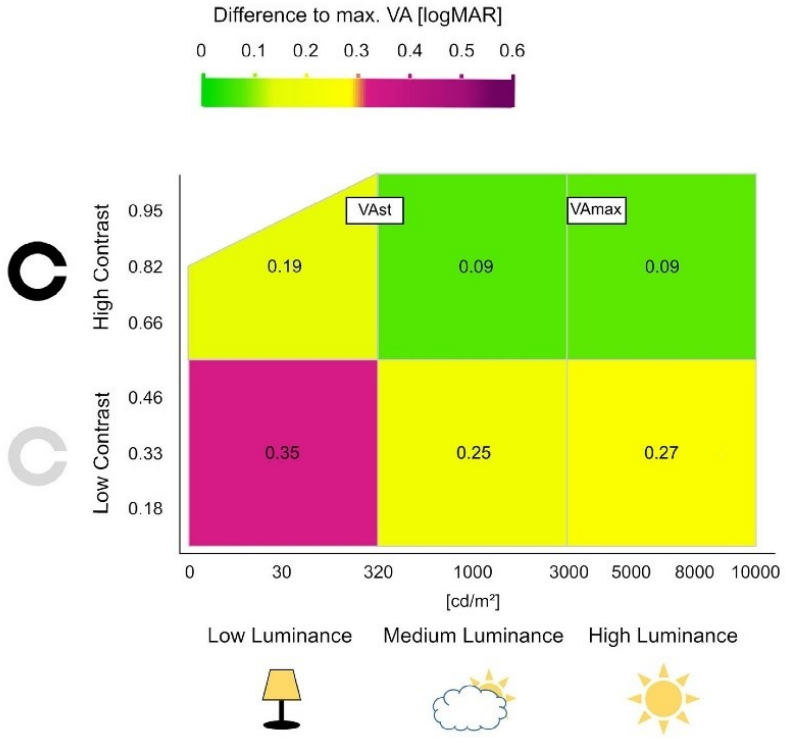

Figure 5. Mean difference in logMAR between the maximum VA and the VA of the respective condition of all participants ($N = 14$). The difference of each VA value for the various conditions to the best VA (mean $VA_{max} = -0.50$ logMAR at C = 95%, median AL = 4000 cd/m^2) was calculated. Each RSI includes certain conditions (contrasts and ambient luminance; see Table 2). These VA differences are averaged accordingly and are written in one representing value in the middle of each RSI. The VA difference is symbolized by different colors (*green* = no/low difference, *yellow* = moderate difference, and *purple* = high difference). The various luminance and contrast levels are clarified by the corresponding symbols. VA_{st} (mean = −0.41 logMAR at C = 95%, AL = 320 cd/m^2) and VA_{max} are shown in white rectangles. Due to technical limitations, VA at 95% contrast could only be determined above AL of 320 cd/m^2.

Discussion

This study demonstrates that the 2D dependence of VA on object contrast and ambient light can be easily assessed. Only testing standard VA (luminance of between 80 and 320 cd/m^2 and maximum optotype contrast)[1] and contrast vision in clinical practice separately do not allow for assessing the full dynamic range of luminance and contrast conditions in everyday indoor and outdoor conditions and thus will miss areas of glare effects. Everyday luminance by far exceeds the standard BCVA condition when the sky is overcast (2000–8000 cd/m^2), and especially when the sky is blue (5000–30,000 cd/m^2).[2] Our measurements on a sunny day (blue sky) have shown that people are confronted with targets, which have much higher luminance (e.g. a white car = 20,000 cd/m^2, a white paper = 13,000 cd/m^2, or a white street sign = 19,000 cd/m^2).

Our study confirms that humans with normal vision reach their VA_{max} at a luminance of 3000 to 5000 cd/m^2, in line with previous observations,[5] with an average improvement of −0.09 logMAR compared to VA_{st}, which approximately corresponds to one line of the ETDRS chart.[6] Thus, clinically determined BCVA underestimates the visual performance of healthy participants.[5] Other studies also found a reduction of VA with decreasing luminance in eye-healthy participants,[26] which is consistent with the lower VA values reached at 0 or 30 cd/m^2 compared to higher ambient luminances in our study. They also figured out that VA for each luminance gradually worsens with decreasing contrast. However, only 0.075 to 75 cd/m^2 were applied as luminance range in the latter study and not to 10,000 cd/m^2 as in our study.

The VA improvement was contrast-independent at higher AL levels, whereas the VA decreased with lower contrasts, as previously reported.[27–29] AL levels above 5000 cd/m^2 led to a slight drop in VA at higher contrasts and a larger drop in VA at lower contrasts. This is caused by scattered light, lowering retinal contrast, and reducing the contrast sensitivity.[30] Higher contrast seem to be more stable against glare,[31] which is confirmed by our results. It should be noted that the atmospheric Rayleigh scattering depends on wavelength, showing an inversely proportional relationship, increasing for short wavelengths compared to long ones.[32] Because there are different wavelengths during the day, there may be increased scattering during the bluish incident light in comparison to other times of the day.

A pupil constriction in relation to increasing luminance is part of the adaptation mechanism of the human eye[33] and, therefore, as in clinical assessment, VA-CAL allowed for natural pupil function. Because we observed the minimum pupil diameter in the VA-CAL test at about 3000 cd/m^2 and above, we neglected the possible effects of retinal illuminance versus luminance, as we were interested in conditions of daily life. However, whereas with dilated pupils more light falls on the retina, reducing diffraction but degrading resolution due to aberrations, small pupils result in a decrease in optical aberrations coupled with a decrease in light scattering; diffraction in turn leads to an increase in light scattering.[34] If pupil size falls below the optimal pupil size for diffraction-limited visual acuity (2.5 mm),[35] diffraction, which is directly proportional to wavelength, is expected to decrease, resulting in reduced VA at subsequent higher luminances. Because the pupil size in our study assumes values only slightly below this optimal size on average (minimum 2.26 mm at 10,000 cd/m^2), VA probably does not drop considerably any further.

Commercial glare tests mostly use point light sources that are not relevant in most daily activities at daylight. Thus, a large luminance background, as used here, describes more closely daily living situations of object viewing. In VA-CAL, adaptation glare[2] is prevented by fade-in time. Absolute glare (>10,000 cd/m^2)[2] also does not occur in VA-CAL. Clinical test devices, like the mesoptometer, usually examine glare sensitivity in the mesopic luminance range with or without stray light.[5,36] In contrast, VA-CAL measures the VA depending on the luminance throughout the photopic range, which better reflects everyday visual conditions.

Sharp presentation of the optotypes, often limited by the monitor resolution, was perfectly guaranteed in the VA-CAL study down to the smallest sizes. Moreover, although charts, such as the Precision Vision Super Vision Test, extends down to visual acuity values of −0.6 logMAR, most of the common charts, like the ETDRS chart we used to check visual acuity in the initial examination, typically end at a value of −0.3 logMAR, often leaving higher visual acuities undetected.[37]

Auditory feedback, like in VA-CAL, serves as a positive motivational effect in these test procedures and is recommended and does not affect the results.[38] Additionally, the presentation of large, above-threshold optotypes at the beginning of each VA measurement (e.g. 0.4 logMAR in VA-CAL), is recommended[39] and the associated correct responses also may contribute to motivation, similar to "easy trials" in FrACT.[8,37]

The test duration in our experimental setup of about 3 hours limits motivation and concentration and is therefore certainly not suited for clinical application. Nevertheless, the overall mean difference (Bland-Altman analysis) between the first and second measurements, although significant, was less than half a letter. Such variations are therefore not clinically relevant as found also with other visual acuity tests with higher values (e.g. FrACT).[40–42] Within the present study, the basic goal was to understand the entire numerical space of VA, contrasts, and luminances first before committing to a smaller space of specific VA measurement conditions for practical purposes.

For clinical application, we are presently developing an abbreviated test version with 16 pairs of Cs and ALs. Based on our extended results, we are using for short version luminance levels of 30, 320, 3000, and 5000 cd/m^2, representing 2 lower and 2 higher luminances common in daily life, which allows quite well to quantitatively describe visual function under conditions of glare in glare-sensitive patients. Further, the improvement of VA pathologies can be detected in the most interesting range from 30 to 5000 cd/m^2, where VA increases in normal observers but decreases in achromatopsia. As in healthy participants, VA values for 82% and 95% contrast were very similar for all luminance levels, we recommend for the short version contrasts of 80%, 50%, and 20%, representing high, middle, and low contrasts. The reduction to such values reduces the test duration to about 25 minutes in total but still allows for an analysis of the most important conditions for discovering pathology that would go unnoticed at regular clinical VA testing.

We found a wide range of normal BCVA (approximately 5 lines; see Fig. 3D) across the continuum of different contrasts and ambient luminances under conditions of daily life. As photoaversion occurs in many optical and neuronal pathologies, it seems

worthwhile to measure VA within a broader range of contrasts and luminances to adequately assess the everyday visual performance of such patients in order to avoid over- or underestimations of their actual eyesight in daily activities. This is especially important in people suffering from glare or night vision problems, like achromatopsia,[3,4,43] or other conditions causing impaired vision, like VA loss at low ambient luminances caused by age-related macular degeneration,[44] early cataract,[45,46] early or advanced keratoconus,[47] or post-refractive surgery, where standard clinical BCVA will miss such conditions strongly debilitating such patients in daily life. Another application is quantification of photophobia, observed in psychiatric diseases and inherited retinal dystrophies.[48,49] The VA-CAL test can well describe photophobia-related VA loss in these patients. It can be expected that BCVA in a patient with an inherited retinal disease with standard BCVA of 0.7 logMAR falls at higher ambient luminances and lower contrasts into a range defined as legal blindness. A possible overestimation of visual performance abilities of these patients, measured under standard conditions, can be avoided by the VA-CAL test. In addition, improvement of visual performance after treatments, probably missed by testing standard BVCA, can be detected and quantified in the VAS assessed by VA-CAL at the higher luminance conditions of everyday life. Defining regions of interest, representing natural conditions, is a suited way for a fast judgment concerning the range of VA values during daily living tasks, where the contrast of viewed objects and ambient light levels are continuously changing. However, as VA is the main parameter determined at different levels of contrast and luminance, a clear and well measurable "space of visual performance" for these parameters can be determined by the VA-CAL test.

In conclusion, our approach to understand and measure the dynamic interactions and correlations among contrast sensitivity, AL, and VA in a combined manner along all three axes was not pursued previously. VA-CAL has been established as a reliable computer-controlled method for assessing VA under widely differing conditions of contrast and ambient luminance common in daily life. In the study population, VA improved initially with increasing ambient luminance, which by far exceeds the defined luminance range of actual clinical VA measurements. The 3D presentation of the VA data results in a VAS extending between the contrast and ambient luminance axes. It illustrates the dynamics of visual performance under varying everyday life conditions and can be useful to detect abnormalities in retinal disorders in glare sensitive patients that would go unnoticed in standard tests of BCVA.

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tvst

Low Vision Rehabilitation

The VA-CAL Test Quantifies Improvement of Visual Acuity in Achromatopsia by Means of Short-Wave Cutoff Filter Glasses in Daily Living Conditions

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Purpose: To quantify visual performance of patients with achromatopsia at various contrast and luminance combinations typical for daily living conditions, in comparison to controls, and to measure beneficial effects of short-wavelength cutoff filter glasses used by patients with achromatopsia to reduce glare sensation.

Methods: Best-corrected visual acuity (BCVA) was tested with Landolt rings using an automated device (VA-CAL test). The visual acuity space was assessed for each participant with and without filter glasses (transmission >550 nm) at 46 contrast–luminance combinations (18%–95%; 0–10,000 cd/m^2). The BCVA differences between both conditions were calculated for each combination as absolute values and relative to individual standard BCVA.

Results: Fourteen achromats (mean ± SD: 37.9 ± 17.6 years) and 14 normally sighted controls (mean ± SD: 25.2 ± 2.8 years) were included in the study. Without filter glasses, achromats' BCVA was best at 30 cd/m^2 (mean ± SEM: 0.76 ± 0.046 logarithm of the minimum angle of resolution [logMAR], contrast = 89%) and worst at 10,000 cd/m^2 (mean ± SEM: 1.41 ± 0.08 logMAR, contrast = 18%), a deterioration up to 0.6 logMAR due to increased luminance and decreased contrast. Filter glasses improved achromats' BCVA for almost all luminances by about 0.2 logMAR but lowered controls' BCVA by about 0.1 logMAR.

Conclusions: The VA-CAL test provides numerical proof that short-wavelength cutoff filter glasses can help patients with achromatopsia in everyday life, avoiding the common situation of severe visual impairment at certain daily object contrasts and ambient luminances.

Translational Relevance: The VA-CAL test discovers losses of spatial resolution in the visual acuity space not seen in standardized BCVA assessment. Filter glasses improve the patients' daily visual performance, rendering them a strongly recommended visual aid in achromatopsia.

Introduction

Achromatopsia is an inherited autosomal recessive retinal disease characterized by a loss of cone photoreceptor function caused by gene mutations,[1–5] mostly in the *CNGA3* or *CNGB3* gene[1–7] (up to 80% of the patients).[4] This manifests itself in four main symptoms typical for this disease: a reduced best-corrected visual acuity (BCVA), photophobia (glare sensitivity), nystagmus, and total color blindness.[1 5] Gene replacement interventional trials in Tuebingen as well as on several more sites worldwide are aiming at developing treatment possibilities, showing so far only a slight improvement of visual acuity (VA) and contrast sensitivity.[2,8] However, to reduce photophobia, most

patients use short-wavelength cutoff filter glasses or tinted contact lenses, blocking short-wave light from the visible spectrum, which is the main factor for photophobia.[9] In this study, we examine the effects of these filter glasses on visual performance by measuring VA at different contrasts and luminances, reflecting daily viewing conditions, and comparing the VA results reached with or without wearing a filter glass. It is known that VA of patients with achromatopsia—also called "achromats" or rod monochromats—is vastly impaired with increasing luminance,[10,11] starting already at approximately 100 cd/m^2,[11] although they report the perception of unbearable glare only at higher luminances. Thus, clinically measured VA determined at standardized conditions (ambient luminance 80–320 cd/m^2 with maximum optotype contrast)[12] is not representative and overestimates VA in daily life situations,[11] in which the ambient luminance already reaches 2000 to 8000 cd/m^2 on cloudy days[13] and thus significantly exceeds the defined luminance range in the clinical VA test. Here we report a more reliable assessment of the visual performance of achromats under daily luminance and contrast conditions by means of the VA-CAL test.[14] In addition, the study presents a new scoring chart for BCVA in a contrast–luminance visual acuity space, which is intended to be used for rapid assessment of visual performance in specific real-world viewing conditions, including those that can cause photophobia. We also can show that short-wavelength cutoff filter glasses are a very useful aid for patients with achromatopsia in daily life, as they prevent legal blindness occurring at contrast and luminance levels typical in daily life.

Materials and Methods

Study Participants

14 achromats (ACHM; aged 16–67 years, mean ± SD: 37.9 ± 17.6 years) and 14 normally sighted controls (aged 21–29 years, mean ± SD: 25.2 ± 2.8 years) underwent the VA-CAL test at the Institute for Ophthalmic Research, Tuebingen, between June 2020 and March 2021. Three of the achromats had biallelic mutations in the *CNGA3* gene and 11 in the *CNGB3* gene.

After signing an informed consent form, BCVA with early treatment diabetic retinopathy study (ETDRS) chart (4 m), slit-lamp examination, optical coherence tomography, and Farnsworth D-15 Color Test was done at an initial ophthalmic examination. Patients with additional eye disorders (e.g., cataracts or post–cataract surgery) were excluded from the study. Controls were healthy individuals with a monocular BCVA of ≥0.8 decimal (0.1 logarithm of the minimum angle of resolution [logMAR]) and no eye disorder. The participants could stop the test at any time. The protocol complied with the Declaration of Helsinki and was accepted by the local ethics committee of the medical faculty of the University in Tuebingen (431/2019BO2).

Procedure

The VA-CAL setup was used to assess BCVA by presenting Landolt rings at a 1-m distance at ambient luminances (ALs) between 0 and 10,000 cd/m^2 with Weber contrasts of 18% to 95%.[14] Ambient luminances were generated by high-power LEDs (Power Flat LED Tapes, 6000K; Solarox Holding GmbH, Dessau-Roßlau, Germany). The target background (5.7-degree light-protected projection surface) had a limited luminance range of 100 to 6800 cd/m^2. This means that under the 320-cd/m^2 condition and from the 8000-cd/m^2 condition, the target background had a slightly different luminance than the ambient light. For all other ambient luminances, the values were similar. VA at 95% contrast was measured only above 320 cd/m^2 because of technical limitations. The QUEST adaptive staircase was used for VA threshold estimation,[15] starting with a Landolt ring at each condition with a visual angle of 0.03 degrees (VA of 0.4 logMAR) for normally sighted controls and a visual angle of 4.16 degrees (VA of 1.6 logMAR) for ACHM.

VA was determined monocularly (eye with better VA or leading eye) without pupil dilation using best correction of refractive errors as ascertained in the BCVA test at 4 m (initial examination). For ACHM aged >40 years, an additional near addition of one diopter was added.[16]

The procedure did not differ from previous investigations with the VA-CAL test (Supplementary Fig. S1).[14] The participants were instructed to indicate the opening direction of the isolated Landolt ring (8 alternative forced choice (AFC)) by wireless keypad as fast as possible (maximum of 10 seconds). A missing response within this time was considered incorrect. Response times (i.e., the time between stimulus presentation and pressing the button on the keypad) were additionally recorded. After completion of the procedure and a subsequent 15-minute break, a second trial was carried out with a short-wavelength cutoff filter glass (PC 550 nm; Multilens, Mölnlycke, Sweden) to check its effect on VA at 46 different contrast–luminance combinations by the same procedure as in the first run. The filter glass was positioned in front of the correcting lenses of the trial frame.

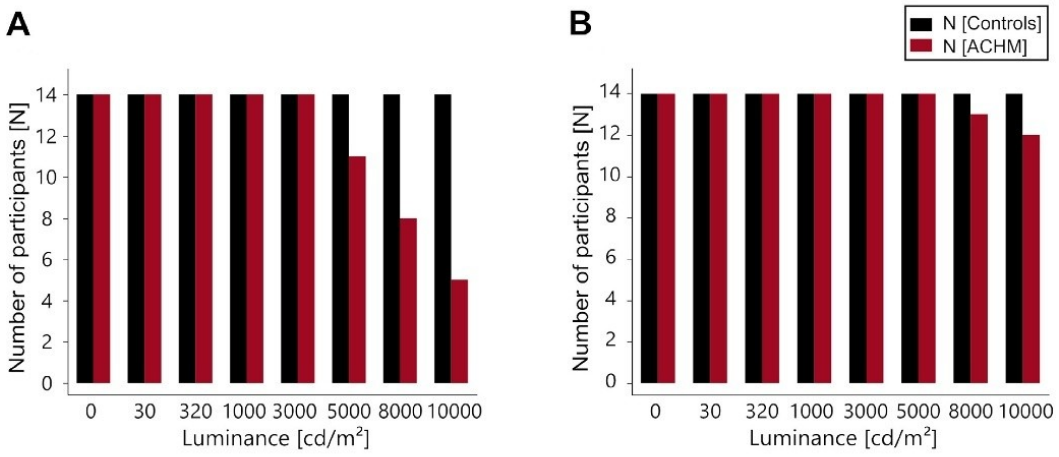


Figure 1. Number of participants completing the test at the various luminance levels. Lenses were added for refractive correction during the test. Two viewing conditions were examined with the VA-CAL test: without (**A**) and with a filter glass (**B**, transmission >550 nm). Controls completed all luminance levels (*black bars* in **A**, **B**), while some achromats had to stop the test at higher luminances without filter glass (*red bars* in **A**) because they could not keep their eyes open due to the high glare or pain. This improved during the run with filter glass (*red bars* in **B**).

Statistical Analysis

Statistical analysis was performed with JMP 15 (SAS Institute, Cary, NC, USA). We investigated the absolute number of normally sighted controls and patients with achromatopsia who completed the different luminance steps (Fig. 1). Descriptive statistics (mean and standard error [SEM] since we did group comparison)[17] of VA logMAR were calculated for controls ($n = 14$, Figs. 2A, 2B, Table) and achromats ($n = 14$, Figs. 2C, 2D, Table). The mean VA of each tested luminance–contrast combination was compared with the mean VA reached at the standard condition according to DIN EN ISO 8596 (VA_{st}; AL = 320 cd/m^2, contrast = 95%) by calculating the VA difference in logMAR (Fig. 3). Normality was checked with the Anderson–Darling test. The results of the controls without a filter glass have already been published[14] and are presented in this study for comparison with the data with a filter glass. Some achromats did not complete the test at high ambient luminances beyond the range of 3000 to 5000 cd/m^2, especially without filter glasses, because they could not keep their eyes open or had pain at a certain luminance (Fig. 1).

A restricted maximum likelihood model was used for analyzing the effect of contrast and ambient luminance (fixed effects) on the participants' (random effect) response times (RTs). Mean RTs for the specific contrast–luminance combinations were used for comparing the effect of the filter glass (Supplementary Table S1). Moreover, the responses were divided into correct or incorrect.

For further analysis, 14 of the 46 contrast–luminance combinations with ALs from 30 to 5000 cd/m and contrasts of 18% to 82% were taken to construct a short version of the test, still including a BCVA condition (AL = 320 cd/m^2, C = 82%) in the range of the standard condition of DIN EN ISO 8596 norm ("standard VA").

The effect of the filter glass on VA under the specific contrast–luminance conditions was calculated by the logMAR differences between each VA measured without and with filter for each participant. Subregions of VA (regions of special interest) were defined by averaging the VA differences of the three adjacent contrast–luminance combinations. Color-coding (green = VA improvement, red = VA deterioration, gray = neither) was used for a graphic illustration that allows the outcome of the test to be quickly grasped (Fig. 4).

Luminous transmittance of the filter glass was calculated by luminance with filter divided by luminance without filter multiplied by a factor of 100.

Pupil diameter was measured by determining the number of pixels along the diameter of the pupil in a picture taken within adaptation phase to each luminance (ImageJ, version 1.8.0; National Institutes of Health, Bethesda, MD, USA) and converting the pixels to millimeters (1 pixel = 0.286 mm). Due to squinting and nystagmus, the pupil diameter could not

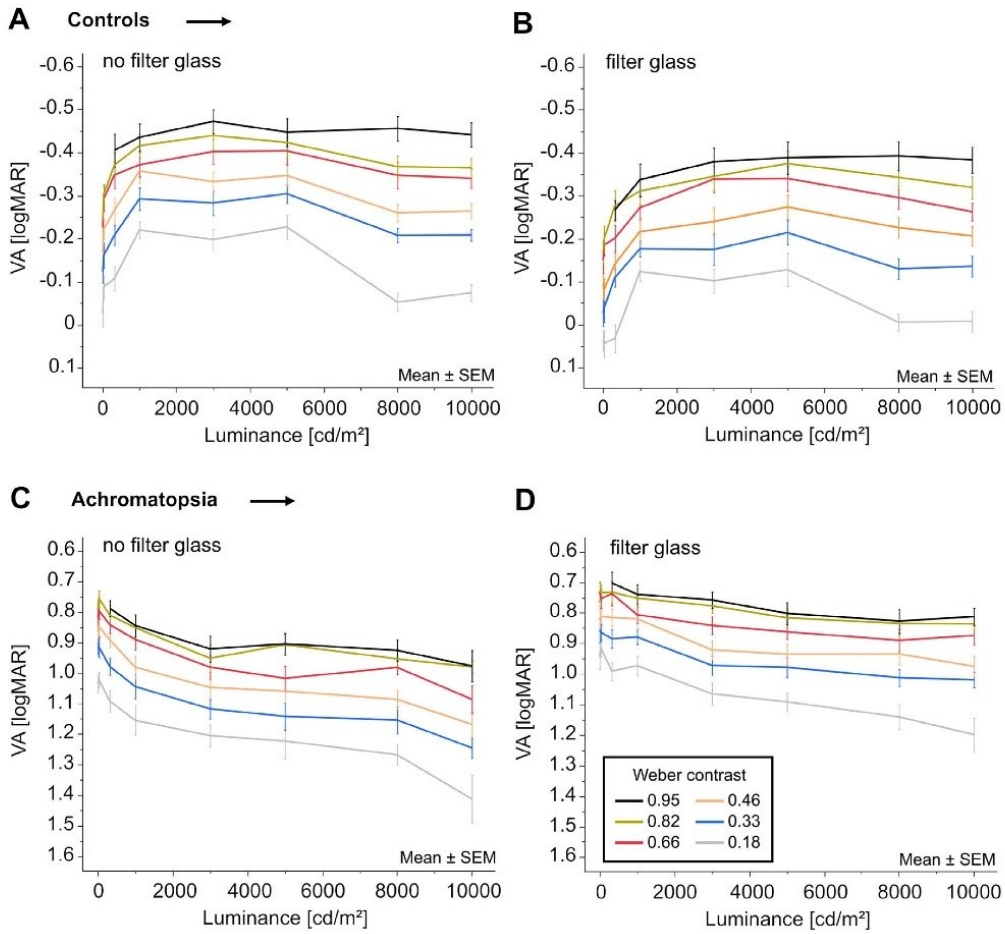


Figure 2. Mean visual acuity thresholds of healthy controls ($n = 14$; **A**, **B**) and achromats (ACHM; $n = 14$; **C**, **D**) determined at different contrasts and ambient luminances. SEM was used for *error bars* (**A–D**). VA was ascertained without filter glass (**A**: controls, **C**: ACHM) as well as with filter glass (**B**: controls, **D**: ACHM). The different contrasts are symbolized by different colors. VA at 95% contrast was measured only above 320 cd/m^2 because of technical limitations. Some of the ACHM stopped the test earlier, by which the mean VA for these luminances was calculated only by the values of the corresponding participants (see Fig. 1).

be measured reliably in all ACHM (Supplementary Tables S2 and S3).

Results

BCVA determined in the ACHM patients at the initial examination (ETDRS chart; luminance = 100 cd/m^2; Weber contrast = 98%) was between 1.3 and 0.7 logMAR (mean ± SEM: 0.84 ± 0.04 logMAR). Spherical refractive errors of ACHM ranged from +10.5 to −9.75 diopters, with cylinders of up to −3.75 (for the distribution of spherical equivalent [sphere + astigmatism/2], see Supplementary Fig. S2A). Controls showed BCVA values between 0 and −0.3 logMAR (mean ± SEM: −0.19 ± 0.03 logMAR) with spherical refractive errors from +2.0 to −3.5 diopters and cylinders up to −1.75 (Supplementary Fig. S2B).

The BCVA values (logMAR) of the controls determined with VA-CAL followed a normal distribution ($P = 0.059$ [with/without filter]), while that of the ACHM subjects did not ($P < 0.0001$ [with/without filter]).

Table and Figure 2 describe mean VA at various luminances and contrasts. Controls showed an improvement in VA up to an AL of 3000 to 5000 cd/m^2 without filter glasses (Fig. 2A).[14] Wearing filter glasses

Table. Data of Normally Sighted Controls and Patients With Achromatopsia

		Controls				ACHM			
		VA Without Filter		VA With Filter		VA Without Filter		VA With Filter	
Ambient Luminance, cd/m^2	Weber Contrast, %	Mean, logMAR	SEM, logMAR	Mean, logMAR	SEM, logMAR	Mean, logMAR	SEM, logMAR	Mean, logMAR	SEM, logMAR
0	82	−0.24	0.03	−0.17	0.03	0.79	0.03	0.73	0.03
0	66	−0.23	0.03	−0.15	0.03	0.82	0.03	0.73	0.03
0	46	−0.17	0.03	−0.10	0.04	0.86	0.03	0.81	0.04
0	33	−0.12	0.03	−0.03	0.03	0.91	0.02	0.86	0.04
0	18	−0.03	0.03	0.04	0.02	1.03	0.03	0.95	0.04
30	82	−0.30	0.02	−0.20	0.03	0.76	0.03	0.73	0.03
30	66	−0.29	0.03	−0.19	0.03	0.80	0.03	0.75	0.03
30	46	−0.22	0.02	−0.08	0.03	0.85	0.03	0.81	0.02
30	33	−0.16	0.03	−0.04	0.03	0.92	0.03	0.86	0.03
30	18	−0.09	0.03	0.04	0.03	1.02	0.03	0.92	0.03
320	95	−0.41	0.04	−0.27	0.02	0.79	0.03	0.70	0.04
320	82	−0.37	0.03	−0.28	0.04	0.81	0.03	0.73	0.03
320	66	−0.35	0.03	−0.20	0.03	0.84	0.03	0.74	0.04
320	46	−0.27	0.03	−0.14	0.03	0.89	0.02	0.82	0.03
320	33	−0.21	0.02	−0.11	0.02	0.98	0.03	0.89	0.03
320	18	−0.11	0.03	0.03	0.03	1.09	0.03	0.99	0.03
1000	95	−0.44	0.03	−0.34	0.04	0.84	0.04	0.74	0.03
1000	82	−0.42	0.03	−0.31	0.03	0.85	0.04	0.75	0.03
1000	66	−0.37	0.03	−0.27	0.03	0.89	0.03	0.81	0.03
1000	46	−0.36	0.03	−0.22	0.03	0.98	0.04	0.82	0.03
1000	33	−0.29	0.03	−0.18	0.02	1.04	0.04	0.88	0.02
1000	18	−0.22	0.02	−0.12	0.02	1.16	0.05	0.97	0.03
3000	95	−0.47	0.03	−0.38	0.03	0.92	0.04	0.76	0.03
3000	82	−0.44	0.03	−0.35	0.03	0.95	0.04	0.78	0.02
3000	66	−0.40	0.03	−0.34	0.03	0.98	0.04	0.84	0.03
3000	46	−0.33	0.02	−0.24	0.03	1.05	0.04	0.92	0.03
3000	33	−0.28	0.03	−0.18	0.04	1.12	0.03	0.97	0.03
3000	18	−0.20	0.02	−0.10	0.03	1.21	0.04	1.07	0.04
5000	95	−0.45	0.03	−0.39	0.04	0.90	0.04	0.80	0.04
5000	82	−0.42	0.03	−0.38	0.03	0.91	0.03	0.82	0.03
5000	66	−0.40	0.03	−0.34	0.03	1.02	0.04	0.86	0.02
5000	46	−0.38	0.02	−0.27	0.03	1.06	0.04	0.94	0.03
5000	33	−0.33	0.02	−0.21	0.03	1.14	0.04	0.98	0.03
5000	18	−0.27	0.03	−0.13	0.04	1.22	0.06	1.09	0.03
8000	95	−0.46	0.03	−0.39	0.03	0.93	0.04	0.83	0.04
8000	82	−0.37	0.02	−0.34	0.03	0.95	0.03	0.83	0.03
8000	66	−0.35	0.03	−0.30	0.03	0.98	0.02	0.89	0.04
8000	46	−0.26	0.02	−0.23	0.02	1.09	0.03	0.93	0.03
8000	33	−0.21	0.02	−0.13	0.02	1.15	0.04	1.01	0.03
8000	18	−0.05	0.02	−0.01	0.02	1.27	0.03	1.14	0.04
10,000	95	−0.44	0.03	−0.38	0.03	0.98	0.05	0.81	0.03
10,000	82	−0.36	0.02	−0.32	0.03	0.98	0.02	0.84	0.02
10,000	66	−0.34	0.02	−0.26	0.02	1.09	0.05	0.87	0.03
10,000	46	−0.26	0.02	−0.21	0.02	1.17	0.04	0.98	0.03
10,000	33	−0.21	0.01	−0.14	0.02	1.25	0.03	1.02	0.03
10,000	18	−0.07	0.02	−0.01	0.02	1.41	0.08	1.20	0.06

Mean values (VA [logMAR]) for specific ambient luminance and contrast conditions of normally sighted controls ($n = 14$) and patients with achromatopsia (ACHM; $n = 14$) determined by VA-CAL without and with wearing a filter glass.

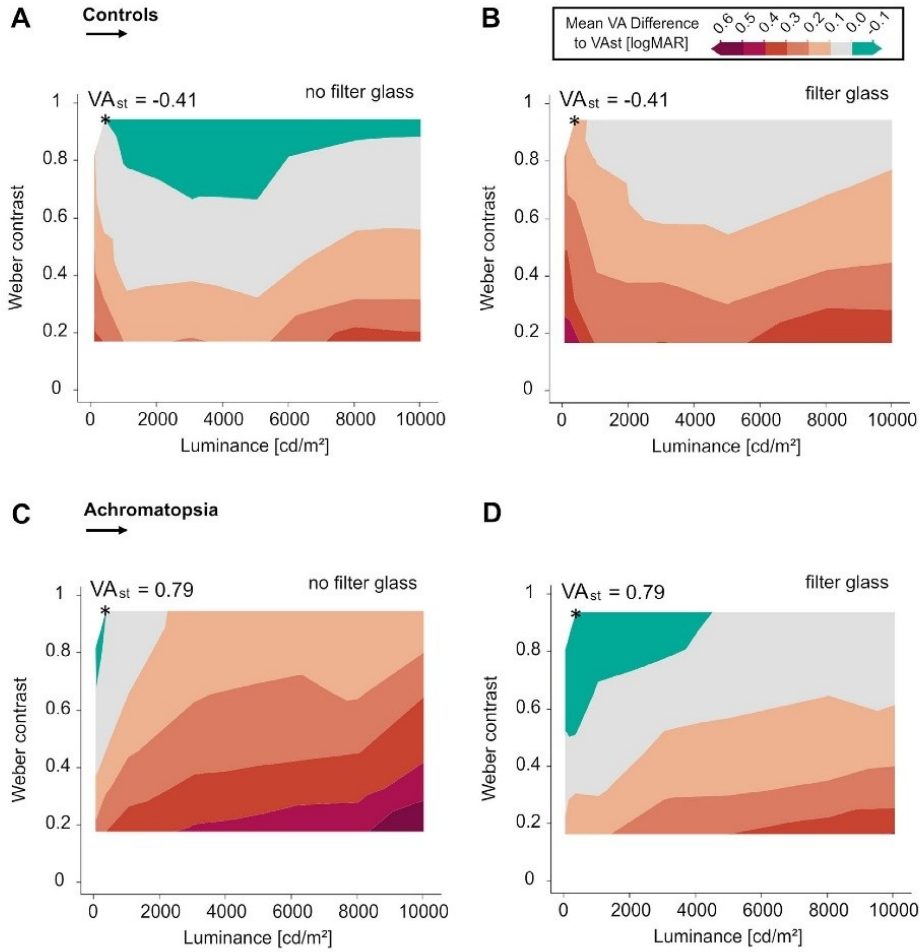
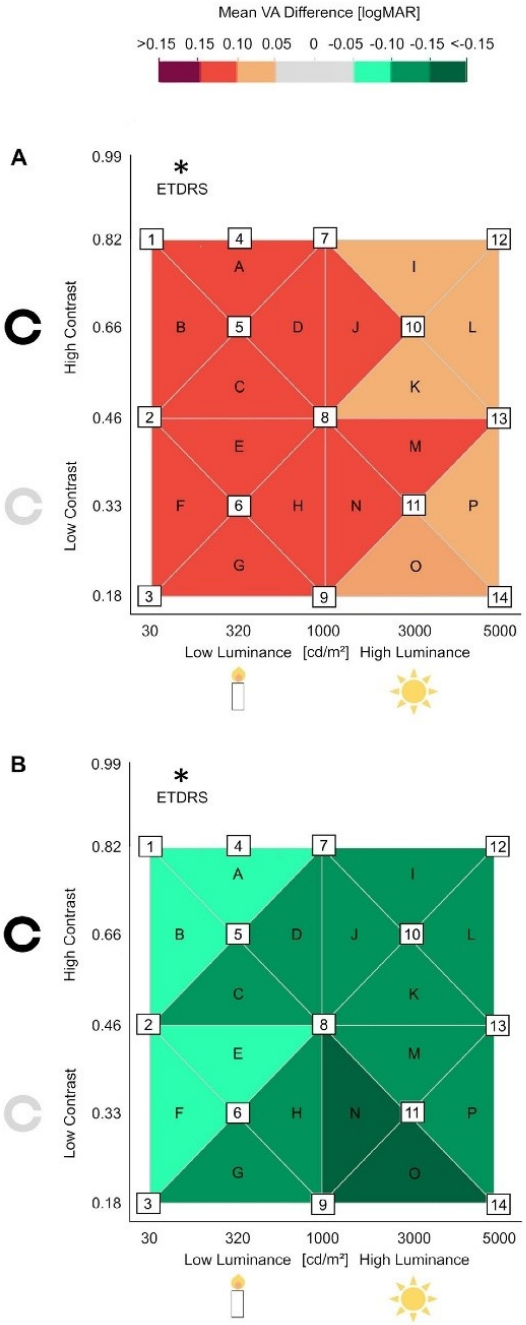


Figure 3. Heatmap of averaged VA (logMAR) difference of each contrast–luminance combination to the standard VA value (VA_{st}, depicted with the *star*, AL = 320 cd/m^2, C = 95%) for controls (**A** = without filter, **B** = with filter) as well as ACHM (**C** = without filter, **D** = with filter). The VA_{st} of the respective participant group reached without filter glass (VAst controls = −0.41 logMAR, VA_{st} ACHM = 0.79 logMAR) was used as a reference for calculation of the difference. The differences are color-coded: *orange to red* = VA worse by 0.1 to 0.6 logMAR than achieved in the standard condition (VA_{st}); *gray* = slightly worse; *green* = better VA than VA_{st}.

worsened the VA of controls in all conditions by about 0.1 logMAR (Fig. 2B). Compared to controls, the VA of ACHM patients was up to 1.5 logMAR worse, particularly at low contrasts and high luminances. Without filter glasses, ACHM reached their best VA at 30 cd/m^2. With increasing luminance, VA decreased by about 0.08 logMAR per 1000 cd/m^2 up to an AL of 3000 cd/m^2, followed by a steady low VA up to an AL of 8000 cd/m^2 and a subsequent drop of VA to a minimum AL of 10,000 cd/m^2 (Fig. 2C). Wearing filter glasses, ACHM improved their VA in all conditions (Fig. 2D), with the highest improvement at higher AL and lower contrasts. The maximum VA was shifted to an AL of 320 cd/m^2. The minimum VA again was reached at an AL of 10,000 cd/m^2. Lower contrast led to a reduction of VA in all luminances.

Figure 3 illustrates the VA differences (color-coded) to the standard VA testing condition (VA_{st}, AL = 320 cd/m^2, contrast = 95%). Without filter glasses, controls had VA values above VA_{st}, especially at high luminances with high contrasts (Fig. 3A). At lower contrasts, VA was worse than VA_{st}, reaching the maximum difference of about 0.4 logMAR at high and low luminances. The use of filter glasses only resulted in losses in the whole luminance–contrast space in relation to VA_{st} (Fig. 3B) in the range of two lines at



TP	Δ VA
1	0.10
2	0.14
3	0.13
4	0.09
5	0.15
6	0.10
7	0.11
8	0.14
9	0.10
10	0.06
11	0.11
12	0.05
13	0.07
14	0.10

RSI	Included measure	Δ VA
A	1,5,7	0.12
B	1,2,5	0.13
C	2,5,8	0.14
D	5,7,8	0.13
E	2,6,8	0.13
F	2,3,6	0.12
G	3,6,9	0.11
H	6,8,9	0.11
I	7,10,12	0.07
J	7,8,10	0.10
K	8,10,13	0.09
L	10,12,13	0.06
M	8,11,13	0.11
N	8,9,11	0.12
O	9,11,14	0.10
P	11,13,14	0.09

TP	Δ VA
1	-0.02
2	-0.04
3	-0.11
4	-0.08
5	-0.11
6	-0.05
7	-0.10
8	-0.16
9	-0.18
10	-0.14
11	-0.15
12	-0.11
13	-0.14
14	-0.13

RSI	Included measure	Δ VA
A	1,5,7	-0.08
B	1,2,5	-0.06
C	2,5,8	-0.10
D	5,7,8	-0.12
E	2,6,8	-0.08
F	2,3,6	-0.07
G	3,6,9	-0.11
H	6,8,9	-0.13
I	7,10,12	-0.12
J	7,8,10	-0.13
K	8,10,13	-0.15
L	10,12,13	-0.13
M	8,11,13	-0.15
N	8,9,11	-0.16
O	9,11,14	-0.15
P	11,13,14	-0.14

Figure 4. Mean difference between the visual acuity with and without the filter glass, for controls (**A**) and achromats (**B**) summarized as VA-CAL score, representing VA under specific contrast–luminance conditions. The VA differences of each participant were calculated first and then averaged. The luminance–contrast conditions were divided in subregions, each containing specific testing points. The corresponding values were averaged by the mean VA difference of with versus without filter glass of the adjacent three testing points/conditions. The mean VA differences for the testing points (TPs) and the subregions (RSI) are presented in the tables on the *right*. TP 4 represents standard VA in VA-CAL short version and was not included in the calculation of the subregions (just three adjacent TPs). The *star* symbolizes the →

←
contrast–luminance combination on which VA is clinically assessed with the standard ETDRS chart. The mean VA differences are symbolized by different colors: *gray* = no/less difference with ±0.05 logMAR; *green* = improvement in VA caused by filter glass; *red* = deterioration of VA caused by filter glass. The different luminance and contrast levels are depicted as different symbols.

medium contrasts, culminating in values greater than the 0.4 logMAR difference. ACHM (Fig. 3C) showed slightly better VA than VA_{st} only at luminances lower than 320 cd/m^2 with high contrasts. In the other conditions, VA was always worse than VA_{st}. With increasing luminance and additionally decreasing contrast, the VA difference to VA_{st} continually decreased up to six lines. Wearing the filter glass improved the VA of ACHM compared with VA_{st} (Fig. 3D). With filter glasses, their VA differences to VA_{st} were smaller than without the filter in the entire luminance–contrast space (Fig. 3D). A VA better than VA_{st} was achieved by ACHM at higher contrasts, now up to 3000 cd/m^2. At lower contrasts, the difference was between 0.1 and 0.2 logMAR. With filter, the maximum difference of 0.41 logMAR to VA_{st} occurred at the highest luminance and lowest contrast. There was an improvement of 0.21 logMAR in this condition compared to without filter.

In Figure 4, based on the extended results, we focused on the most critical conditions of daily life. The VA difference caused by the filter was calculated, showing how the filter affected the VA in defined luminance–contrast subregions (color-coded). In controls (Fig. 4A), VA was reduced by the filter glass in each subregion. The deterioration was smallest at high luminances with high contrasts and greatest at low luminances no matter if low or high contrasts. The mean VA difference (VA-CAL score) ranged from 0.06 logMAR (subregion L) to 0.14 logMAR (subregion C). In ACHM (Fig. 4B), on the other hand, VA improved in each subregion with the filter glass. The VA difference was smallest at low luminances with high contrasts and greatest at high luminances with low contrasts. The greatest VA improvement was −0.16 logMAR (subregion N), while the smallest VA improvement was −0.05 logMAR (subregion B).

Response times of ACHM were highly significantly affected by AL ($P < 0.0001$) and by contrast ($P = 0.0008$), both with and without filter ($P < 0.0001$ for both parameters). In both viewing conditions, RTs became longer with increasing AL and decreasing contrast (Supplementary Table S1). Without filter, RTs increased over all contrast on average by 41.3 (95% confidence interval [CI], 34.9−47.8) ms per 1000 cd/m^2, with filter by 32.5 (95% CI, 27.2−37.9) ms. Thus, the filter glass caused an RT improvement of about 9 ms per 1000 cd/m^2. Values of incorrect responses were 150 ms longer on average than correct answers without filter and 250 ms with filter (Supplementary Fig. S3).

Pupil diameter of ACHM already was 2 mm smaller than in the control group at the minimum AL of 0 cd/m^2. The pupil diameter of ACHM decreased with a higher luminance by about 1 mm at 320 cd/m^2, followed by another decline up to 5000 cd/m^2. With filter glasses, the mean pupil diameter was larger in both groups in all conditions, again showing a reduction with increasing luminance (Supplementary Tables S2 and S3).

Luminous transmittance of the filter glass for the condition with 0 cd/m^2 ambient luminance, meaning only the presence of the target background with a luminance of 100 cd/m^2, was about 22%. For the condition with 3000 cd/m^2 ambient luminance, the luminous transmittance of the filter glass was 29%.

Discussion

We investigated the effect of short-wavelength cutoff filter glasses on the visual acuity of achromats and healthy controls at different conditions of contrasts and ambient luminance using the VA-CAL test, which allows a more realistic, close to everyday life condition evaluation of the visual performance. With the conventional clinical determination of BCVA (e.g., using the ETDRS chart),[18] measurements are only performed with a fixed luminance (80–320 cd/m^2) and maximum optotype contrast,[12] covering only a very small range of conditions of daily life. Our results show that the VA of achromats continuously decreases with increasing luminance, reaching the status of moderate to severe visual impairment (0.5−1.3 logMAR).[19] Compared to the achromats' VA at the standard condition, this leads to a worsening of VA of about six lines. The clinically measured VA, therefore, is often overestimated and better than it is in patients' daily living conditions, which was also found in previous studies.[11] Controls also showed a four-line drop in VA to standard condition with lowest contrast and highest luminance. In controls, glare thus seems to occur above 8000 cd/m^2, which reduces their visual performance. Thus, controls show a higher resistance to glare compared to achromats. VA changes take a different course when increasing the luminance to approximately 3000 cd/m^2, leading to an improvement

in VA in controls at all contrasts, while achromats show a steady decline.

At the level where achromats' vision decreases with higher luminances, some patients use the term *glare* already at moderate luminance levels, showing first signs of squinting and lid closure, although most objective signs of glare (frequent lid closure, pain, inability to see large Landolt rings) occur only above luminance levels of 3000 to 5000 cd/m^2 (Fig. 1B). Loss of VA is therefore part of the disorder that does not allow proper information processing of rod signals in the retina even at luminance levels below values where photophobia prevents further testing.

Photophobia in achromats and their generally poor VA can be explained by the inherited condition of nonfunctioning cone photoreceptors.[1,2,4,5,20,21] According to achromats in this study, photophopia was also the reason why they wanted to stop the measurement at a certain luminance level without filter glasses. As a direct aid against sensation of glare, patients often use short-wavelength cutoff filter glasses, which filter out the glare-causing short wavelengths.[9] Other studies showed reduced photophobia and improved VA when using tinted lenses.[22–24] Almost all achromats (12 of 14) could handle the highest glare of 10,000 cd/m^2 in this study with filter, whereas without the filter glass, only 5 of 14 achromats continued up to the highest levels tested. The filter glass apparently protects from subjective glare sensitivity and the associated feeling of discomfort. Another indication of increasing glare is the rising response time with higher luminances that was found in this study. This was improved by wearing the filter glass, which may lead to faster orientation in daily environments.

Using the filter glass, the VA of achromats improved over all luminance–contrast combinations. Especially at high luminances, the mean VA of ACHM was up to 0.23 logMAR better than without wearing a filter glass. We also could confirm previous studies that described an increased contrast sensitivity in achromats when using filter glasses, which most likely also contributes to the improvement of VA.[9,22] Improvement of VA at higher luminances was also shown for other retinal diseases like retinitis pigmentosa.[25] Examples from everyday life illustrate how often one is confronted with such high luminances. Own measurements have shown that a Caucasian face already has 8000 cd/m^2 in the sun. The filter glass could thus also help in facial recognition. A white car in the sun has a luminance of 20,000 cd/m^2, and hence, potential glare and danger when crossing the street can be reduced with the filter glass. Moreover, road signs that reach up to 19,000 cd/m^2 in the sun could be better read and traffic lights, with luminances of between 2000 and 8000 cd/m^2,[13] could be better recognized, even though the problem of color vision still arises here. A filter glass can thus substantially help achromats in all kinds of everyday situations, both in visual performance and for general well-being.

It may seem that normal sunglasses could simply be used to absorb the entire light spectrum and thus prevent saturation of the rods of achromats. Furthermore, there is some probability that neutral density filters of similar absorption for white light achieve the same effect. However, blocking short-wavelength light may have beneficial effects by avoiding chromatic aberration and straylight by activation of autofluorescence from the natural lens, induced by blue light in middle-aged and older adults. Nevertheless, the maximum sensitivity of rods is in the short-wavelength region of the visible spectrum, so a filter that passes only long-wavelength light is well suited.[9] In addition, there are incomplete achromatopsias, in which some cone types function partially,[26] and it cannot be excluded that even in complete achromats, some cones still exist. Thus, these existing cones could be stimulated while reducing the light exposure of the rods.[9]

The filter glass used here (transmission >550 nm) is very well suited. It can be worn in any daily luminance situation without having to change it constantly, especially since, as shown in this study, it has a positive effect on achromatic VA at almost all luminances. Using individually selected filter glasses, as recommended,[9] may have resulted in an even higher improvement of VA in some achromats.

The VA of the normal controls improved with increasing luminance, as shown in other studies.[27] However, when using short-wavelength cutoff filter glasses, they showed a deterioration of VA for all conditions. This may be explained by the fact that the filter glass reduces the retinal illumination, an effect that in achromats is masked by the degree of improvement. Thus, the gain of VA in such conditions in achromats not only compensates this physiologic loss but also surpasses it by a further gain of almost two lines.

Subregions representing specific luminance and contrast conditions can be used for assessing VA changes by interventions in clinical studies (VA-CAL scoring chart), for example, in the *CNGA3* gene replacement therapy trial targeting achromatopsia.[2,8] For a short version, focusing on the most critical conditions of daily life, we chose luminances from 30 to 5000 cd/m^2, ensuring that patients could complete the test. The reduced range still allows the identification of typical VA performances and inferences of pathology. This will also result in a shorter total test duration of about 25 minutes per eye but still allows for an analysis of the results in different levels

of abstraction (overall mean, quadrants, subregions, single contrast/luminance conditions).

In conclusion, testing the BCVA of achromats in a range of critical contrast and ambient luminances by means of the VA-CAL test provides a reliable assessment of visual performance in daily life that is not possible with the clinical standard BCVA test alone. With increasing luminance and decreasing contrast, the VA of achromats can deteriorate by about six lines compared to the standard condition. Short-wavelength cutoff filter glasses proved to be a very useful aid for achromats, improving VA across all contrast–luminance combinations. Especially at higher luminances, the VA of achromats was up to two lines better than without filter glasses, thus avoiding the severe visual impairment that normally occurs in achromatopsia at higher luminances.

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The Impact of Glare Type and Intensity on Objective and Subjective Visual Performance

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ABSTRACT

Purpose To compare the effects of spatially uniform glare and point light sources on visual acuity (VA) of individuals with normal vision under everyday contrast and illuminance conditions, and to investigate the related subjective perception of glare.

Methods VA was assessed with spatially uniform glare (120 cm x 120 cm) lighting (VA-CAL test) and with four point light sources in either the paracentral (13.3°) or the near-peripheral visual field (23.5°). For all conditions, the illuminance and the optotype contrast (Landolt rings) were varied in four steps from 25 to 2200 lux and five steps from 20% to 80%, respectively. In addition to visual acuity testing, the subjective glare discomfort score was assessed for each illuminance using the Photoaversion Severity Questionnaire (PSQ).

Results Twelve volunteers with normal vision (22 to 32 years, 6 women, 6 men) were enrolled in the study. Overall, regardless of the type of glare, increasing illuminance improved VA, while decreasing the contrast reduced VA. A statistically significant difference of 0.06 logMAR for the different types of glare was found only between uniform and point light glare in the near-periphery. The discomfort scores increased with illuminance, but did not differ statistically significantly between the different types of glare.

Conclusions Both uniform and point light sources are a good way to measure daily visual performance in glare and show comparable results in influencing VA and subjective discomfort in everyday conditions.

Translational Relevance Uniform light sources are just as suitable for testing visual acuity under glare as point light sources, although we recommend using uniform light for assessing daytime performance and punctual light for testing fitness to drive at night.

Key words Visual acuity, light sources, glare, visual performance

INTRODUCTION

Visual acuity, as the most comprehensive and easily obtained parameter, plays an important role in the assessment of visual performance and is dependent on a number of factors, including contrast, ambient lighting, and glare. While these parameters are well defined for standardized acuity testing, in the real world these parameters are not constant, but are continually changing, as is visual acuity. Conventional visual acuity tests, such as the ETDRS chart [1], only measure visual acuity at a specific level of ambient light and at maximum contrast [2]. However, it has been shown that visual acuity improves with increasing luminance in individuals with normal vision [3,4]. In everyday life, our visual system must deal with a wide variety of light sources, ranging from small and bright point light glare such as oncoming car headlights or street lights at night [5, 6, 7], to large, uniform glare such as windows [8], reflective walls, street signs, sky on horizon, or sunlit snow patches in winter. Since the latter type of glare, point light glare, is of particular concern in traffic safety research, commercially available instruments such as mesoptometers or the nyctometers, can be used to test contrast vision in dim light with glare from point light sources [9]. In contrast, there are only a few studies on the effects of spatially uniform glare. Our group developed the Tuebingen VA-CAL test for measuring visual acuity under different levels of contrast and ambient luminance [10,11]. It uses a surface-emitting light source for a diffuse glare in the range of 25 to 2,200 lux as it can be found in everyday life, such as reflections of bright lights on walls, the overcast sky, road or information signs, either sunlit or self-illuminated. All of these lighting conditions share in common the necessity to allow the detection of different levels of contrast. We have recently found that many combinations of contrast and ambient luminance in daily living condition impact visual acuity in both healthy individuals and patients suffering from retinal disorders to various degrees [10,11]. To our knowledge, no study has directly compared the effects of point source and spatially uniform glare on visual acuity and subjective discomfort. This study examines how these different types of glare affect visual performance by assessing visual acuity at varying contrast levels and illuminance conditions representative of everyday life. Specifically, we compare point light sources, either paracentral or near-peripheral, with

spatially uniform light sources. In addition, we investigate the effect of these light sources on subjective glare discomfort using the Photoaversion Severity Questionnaire.

MATERIALS AND METHODS

Experimental Setup

Visual acuity was determined at five contrast and six illuminance levels using a modified prototype (M&S Technologies, Niles, USA) implementing the VA-CAL-procedure described elsewhere [10]. For spatially uniform glare, four commercially available dimmable LED panels (each 60x60 cm, 60 W, 5500 – 6000 K; chromaticity: 0.313, 0.342; Prismica S.L., Valencia, Spain) were used, controlled using a computerized LED driver (IL-D53DALI2; Interlight GmbH, Arnsberg, Germany) to produce illuminances from 25 to 2,200 lux at the test distance of one meter. Optotypes (Landolt C rings) were presented on a high-resolution display (Microsoft Surface Pro 7; Microsoft Corporation, Redmond, Washington, United States), mounted in the center of the panels (Figure 1a). For point light a commercially available glare testing system (Glare Testing System, M&S Technologies, Niles, USA) was modified to include paracentral (13.3°) and the near-peripheral point light glare (23.5°). The CIE xy chromaticity of the LED spotlights is (0.454, 0.413), the illuminance ranges match those of LED panels (Figure 1b). To avoid reflections from the glare lights from walls or ceiling, black non-reflective folding screens were placed around the setups. For near-peripheral point light glare, the illuminance level was limited to 1400 lx due to technical limitations.

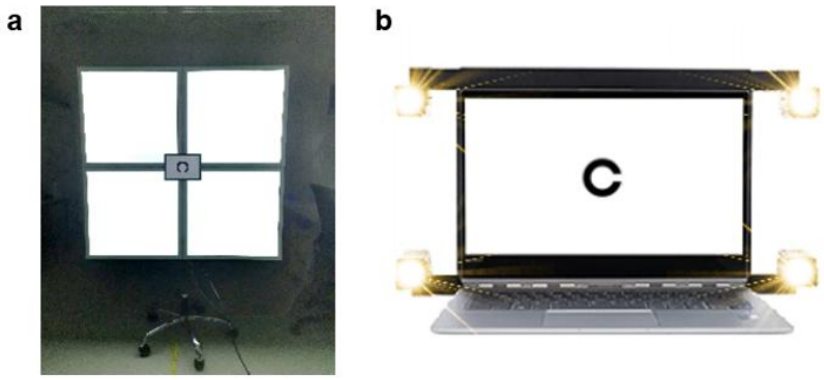

Figure 1 *Experimental setup. a) Photograph of the VA-CAL prototype featuring four LED panels and a high-resolution screen for presenting optotypes; b) Sketch of the modified CTS VA testing system with four point light LEDs for paracentral glare.*

Study Participants

Twelve volunteers (6 female, 6 male) aged 22 to 32 years (mean ± SEM: 28.1 ± 2.7 years) were recruited from the student body of the University of Tübingen and the staff of the University Eye Hospital Tübingen and enrolled in the study after confirmation of the inclusion and exclusion criteria. Best-corrected visual acuity (BCVA) was assessed using a standardized ETDRS-chart (4 m, 100 cd/m², 98% contrast) in a preliminary examination to ensure the inclusion criterion of a monocular visual acuity of at least 0.1 logMAR. Participants with ocular diseases were excluded. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Medicine, University of Tübingen (431/2019BO2). All participants received detailed information about the study and provided written informed consent.

Experimental Procedure

Participants were best corrected with an addition of +0.75 diopter to correct for near distance testing and were seated in a darkened room at a distance of one meter in front of the stimulation devices in a combined chin and head rest. After an initial 5-minute dark adaptation period during which instructions were given, five levels of illumination were presented in ascending order of intensity. A one-minute adaptation period was added before each

illumination level, during which the participants were asked to fixate a red fixation cross (2.9°) in the center of the screen and to rate their subjective discomfort with the current glare condition between 0 and 10 (0 = no discomfort/pain; 10 = unbearable discomfort/pain) using the Photoaversion Severity Questionnaire, an extended version of the de Boer rating scale for discomfort glare [12]. At each illumination level, Landolt C rings of varying size were presented monocularly, and their size was controlled by an adaptive staircase procedure, while their orientation was randomly chosen from eight possible directions. Depending on the illumination level, the procedure was repeated for either two or three contrast levels (Weber 80%, 65%, 50%, 35% or 20%; Fig. 2), respectively, resulting in a total 13 visual acuity values. Participants had to indicate the direction of the opening of the Landolt C ring using a wireless keypad within a maximum of seven seconds. Failure to respond within this time or providing an incorrect answer was counted as a wrong response (8-alternative forced-choice). If the direction could not be identified, the participants were instructed to guess the direction. An auditory feedback was provided. The procedure ends, when the maximum attainable visual acuity is determined [13].

Participants were randomly assigned to begin the experiment with either spatially uniform glare or point light glare. For point light glare, the paracentral glare condition was performed first, followed by the near-peripheral glare condition.

Statistical analysis

To investigate the effects of the different glare types on VA under different levels of contrast and ambient luminance, a full-factorial linear mixed-effects model was employed, with the fixed factors being condition (light sources/levels: paracentral, near-peripheral, uniform glare), the continuous contrast level, and the continuous logarithmized illuminance, both modeled as quadratic terms. The participant was treated as a random effect. The model was fitted using restricted maximum likelihood (REML). The variance inflation factors (VIF) of the predictors were calculated and assured to fall well below the common threshold value, indicating no collinearity between them [14]. The models' residuals were confirmed visually to follow a

normal distribution and the homogeneity of the variances was ensured using the Brown–Forsythe test and reported in case of violations [15,16]. Post hoc comparisons of the least-squares means using two-tailed t-tests were conducted in case of statistically significant effects. One participant was unable to take part in the peripheral measurement for personal reasons, meaning that only 11 people were considered here.

The participants' discomfort score regarding the Photoaversion Severity Question were analyzed using a full-factorial generalized mixed model with ordered beta regression [17] (estimated using maximum likelihood), with the fixed effects glare condition (light sources/levels: paracentral, near-peripheral, uniform glare) and illuminance (continuous). To account for repeated measurements and unequal group sizes the participant was included as random effect.

Statistical analyses were performed using JMP Pro 17 (SAS Institute, Cary, United States) or the R Statistical language (version 4.2.2; [18]), using the packages marginaleffects (version 0.14.0; [19]) and glmmTMB (version 1.1.7; [20]). If not otherwise stated, an alpha level of 0.05 was used for all statistical analyses.

RESULTS

The mean participants' BCVA determined with the standard ETDRS-chart (4 m; luminance = 100 cd/m²; contrast = 98%) was between -0.1 and -0.3 logMAR (mean ± SEM: -0.18 ± 0.10 logMAR).

Figure 2 shows how visual acuity depends on the different glare types (uniform, near-peripheral, paracentral) at different illuminances and contrasts. The pattern of least-square means VA as a function of illuminance and contrast was similar for all glare types (Figure 2). Increasing the illuminance up to approximately 750 lx improved the VA on average, while decreasing the contrast deteriorated mean VA regardless of illuminance. The linear mixed-effects model revealed statistically significant effects of illuminance, contrast (both $p < 0.0001$), and type of glare ($p = 0.0482$) on VA as shown in Table 1. A post hoc paired t-test revealed a

statistically significant mean difference of 0.06 logMAR between uniform glare and near-peripheral point light glare (Table 2), but not between paracentral and near-peripheral point light as well as uniform light and paracentral point light.

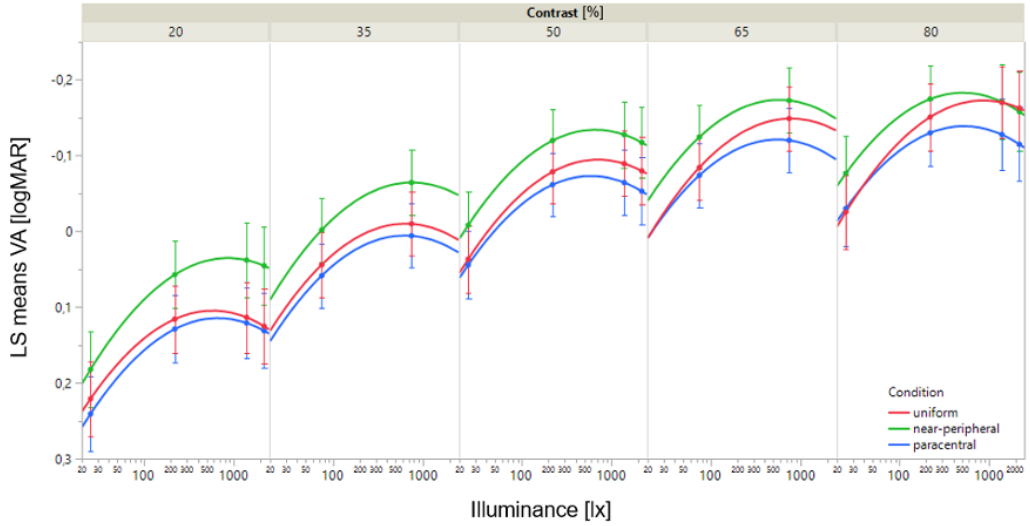

Figure 2 *Visual acuity as a function of different types of glare, illuminance, and contrast as predicted from the linear mixed-effects model. With LS (Least Square) means VA [logMAR] on y-axis and illuminance on x-axis. The VA curves of the individual contrasts (20-80%) are shown separately and indicated by columns in ascending order from left to right. The different colors of the curves represent the different conditions (red = uniform glare, green = near-peripheral point light glare, blue = paracentral point light glare. The error bars indicate the 95% confidence interval at the tested combinations of illuminance and contrast.*

Table 1 *Results of the linear mixed-effects model (n = 490, R2adj. = 0.8133) with the dependent variable visual acuity and the random effect participant.*

Effect	*F*-statistic	*p*-value
Log(Illuminance)	F(1, 465) = 100.5065	<.0001***
Contrast	F(1, 465) = 101.2676	<.0001***
Glare type	F(2, 465) = 3.0513	.0482*
Log(Illuminance)*Contrast	F(1, 465) = 0.8239	.3645
Log(Illuminance)* Glare type	F(2, 465) = 0.7464	.6047
Contrast*Glare type	F(2, 465) = 1.4713	.3894
Log(Illuminance)*Contrast*Glare type	F(2, 465) = 2.2823	.1687
Log(Illuminance)*Log(Illuminance)	F(1, 465) = 72.3179	<.0001***
Contrast*Contrast	F(1, 465) = 136.2783	<.0001***

Alpha level = 0.05; asterisks indicate the level of significance: *p < .05, **p < .01, ***p < .001

Table 2 *Results of post hoc comparisons using paired t-tests of the least-squares means obtained from the linear mixed-effects model. Each glare type was compared with another and the mean VA difference between them was calculated.*

Comparison	Difference [95% CI] (logMAR)	*t*-statistic	*p*-value
uniform – near-peripheral	0.06 [0.01, 0.11]	*t*(465.0595) = 2.3485	.0193*
paracentral – near-peripheral	0.05 [0.00, 0.10]	*t*(465.0595) = 1.9492	.0519
uniform - paracentral	0.01[-0.04, 0.06]	*t*(465.0171) = 0.4255	.6707

Alpha level = 0.05; asterisks indicate the level of significance: *p < .05, **p < .01, ***p < .001

Figure 3 shows the glare discomfort ratings obtained from the Photoaversion Severity Questionnaire (y-axis) for different types of glare (colored lines) and illuminance levels (x-axis). As expected, the generalized linear mixed model revealed a statistically significant effect of illuminance on discomfort scores (Table 3), with higher illuminance levels leading to greater discomfort regardless of the type of glare. For all illuminances, the uniform light source was rated as the most comfortable, followed by the near-peripheral and paracentral point sources. However, there was no statistically significant effect between the different types of glare in terms of discomfort.

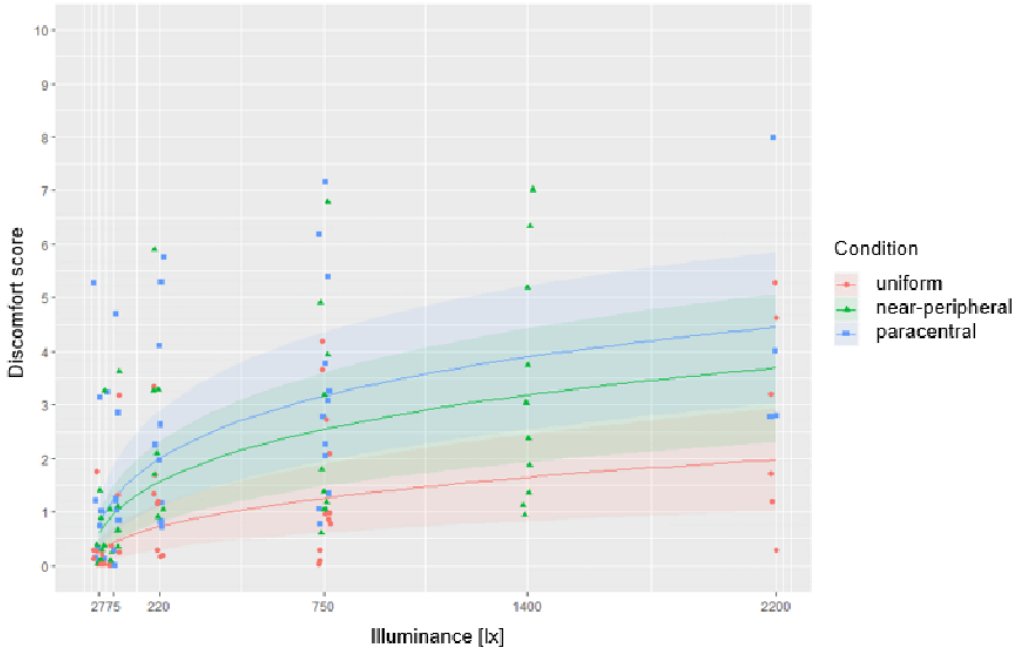

Figure 3 *Discomfort scores of the Photoaversion Severity Questionnaire as a function of illuminance and glare type (symbols) and prediction of the ordered beta regression (lines). Colors represent the different types of glare, shaded bands 95% confidence intervals of the prediction.*

Table 3 *Results of the generalized linear mixed model with ordered beta regression (n = 175, dispersion parameter = 21.4). The model's intercept corresponds to uniform glare at an illuminance of 0 lx.*

Effect	Estimate (SE)	*z*-Value	*p*-value
(Intercept)	-5.253 (0.670)	-7.836	<.001***
paracentral	0.874 (0.720)	1.214	.225
near-peripheral	1.123 (0.669)	1.680	.093
log(Illuminance)	0.501 (0.090)	5.560	<.001***
paracentral*log(Illuminance)	-0.002 (0.110)	-0.015	.988
near-peripheral*log(Illuminance)	0.007 (0.007)	0.068	.946

Alpha level = 0.05; asterisks indicate the level of significance: *p < .05, **p < .01, ***p < .001

DISCUSSION

In a previous study, we demonstrated that visual acuity is not constant and represented by a single value [4], as suggested by the well-established clinical standard [2]. Instead, visual acuity varies continuously with contrast and illuminance [4]. Conventional visual acuity testing, in which visual acuity is assessed at maximum contrast at a given illuminance [1,2], is therefore unable to describe visual acuity in everyday situations with constantly changing contrast and illuminance conditions and is essentially limited to an artificial condition. Visual acuity decreases especially under glare and low contrast conditions [3,4], which may lead to overestimation of visual acuity, especially in patients who are sensitive to glare [11]. In this study we investigated the effect of different glare types and varying contrasts on visual acuity (disability glare), and on subjective glare perception (discomfort glare). Contrary to our intuitive hypothesis that point light glare would lead to both greater discomfort and increased disability glare, our results did not generally confirm this. While no statistically significant difference was found between the different types of glare on the Photoaversion Severity Questionnaire discomfort score, a small but statistically significant reduction in visual acuity was found for near-peripheral point source glare (23.5°) compared to uniform glare, but not between near-peripheral and paracentral (13.3°) or paracentral and uniform glare. Interestingly, the increase in disability glare seems to have no effect on discomfort glare in our young population of volunteers, although Lin and colleagues describe a correlation between glare angle and subjective glare perception for angles ≥ 10° [21].

One would expect that a uniform diffuse light source would illuminate the retina more evenly than point sources, which stimulate only small areas of the retina, resulting in increased discomfort and disability glare. However, the results of this study contradict this hypothesis in young healthy adults, at least for the particular conditions tested. Further factors influencing glare in addition to the light intensity and shape (uniform vs. point source) of the light sources are the size and number of light sources, the position in the field of vision and the adaptation state of the retina [22].

Sivak et al. [23] showed that the area of the light source affects glare discomfort: smaller light sources produce the same brightness over a smaller area, so the brightness is locally more intense. However, point sources of light are not imaged as "dots" on the photoreceptor mosaic; rather, the light is distributed across the retina by diffraction and imperfections in the eye's optics and scattering [24]. Future research needs to focus on possible differences in the effects of uniform and point glare on disability glare and, in particular, discomfort glare in patients with cataracts, as these are known to show significant disability glare and reduced contrast sensitivity [25], which affects their fitness to drive [26], among other problems.

The area and shape of the light source also affects the retina's state of adaptation [24, 27]. A large uniform light source is likely to provide better light adaptation than comparably small point light sources, especially considering that intrinsically photosensitive retinal ganglion cells (ipRGCs) are non-image-forming encoders of ambient light [28]. However, multiple point light sources in the field of view may counteract this effect, possibly explaining the absence of differences between glare conditions in our study. In nighttime road traffic, multiple point light sources contribute to visual interference, particularly from oncoming vehicles. Conventional glare tests typically employ only a single point light source [9], possibly resulting in increased discomfort and disability glare. It should also be noted that previous studies investigating discomfort glare were conducted under scotopic or mesopic conditions, with background luminance limited to 3 cd/m² [29, 30], or under low-luminance photopic conditions, with ambient luminance limited to < 100 cd/m² [27], and therefore their results are not directly comparable to ours, as studies at high luminance levels are missing.

In addition to the number of point sources, their position in the visual field also plays an important role. Interestingly, as mentioned above, Lin et al. found that a glare source at 10° from the line of sight caused slightly more discomfort than a source at 20° [21], whereas in our study we found no difference in either discomfort glare or disability glare between near-peripheral (23.5°) and paracentral (13.3°) point light sources. Jones et al. describe a reduction in contrast sensitivity under scotopic glare conditions (0.32 cd/m²) for a point light source of

0.25° diameter at 3° eccentricity [31], but did not compare different eccentricities. In a study comparing high intensity discharge (HID) and halogen head lamps, Bullough and colleagues found statistically significant effects of eccentricity (5° vs. 10°) on both discomfort and disability glare (measured as contrast sensitivity) independent of lamp type, with worse values for the smaller eccentricity [32] Further research should investigate the effect of glare light source eccentricity on both glare discomfort and disability, especially in the central visual field. To our knowledge, no studies have addressed this aspect.

Bullough et al. also report a statistically significant effect of lamp type on glare discomfort, namely stronger discomfort ratings with HID lamps, which is white-blue, compared to halogen and blue-filtered halogen lamps, which are rather yellowish, independent of the illuminances [32]. They attributed the greater discomfort to the higher energy in the short-wavelength range of the visible spectrum, where blue cones are most sensitive. Interestingly, this seems to have no effect on glare disability [32]. These findings were confirmed by Flannagan et al. who found the lowest discomfort ratings for yellowish light sources with a peak wavelength of 577 nm [29, 33].

However, the results of Bullough et al. and Flannagan et al. also point to a limitation of our study, which used different color temperatures: the uniform glare is produced by white-blueish LEDs behind a diffusing screen, while the point light sources produce a warm, yellowish light. This difference in color temperature may also partially explain the results of our study and should be investigated further.

Another limitation of our study is the young, ocularly healthy study population. Older individuals may exhibit a greater effect of point light sources on visual acuity because age-related factors such as dry eye disease and lens opacities (e.g., cataracts) can increase light scattering [34-36]. Similarly, certain clinical conditions, such as achromatopsia [37, 38] and congenital stationary night blindness [39], are associated with cone dysfunction and pronounced photophobia, which may exacerbate glare sensitivity. While previous research has demonstrated impairment in achromats under uniform lighting conditions [11], their response

to point light sources remains unstudied. In addition, individual differences in light perception were observed in our study. Increasing the sample size may help to account for such variability. Therefore, further research is needed, especially with different groups of participants.

In summary, both glare conditions are necessary to fully evaluate visual performance in everyday life. While VA-CAL with uniform glare primarily simulates daylight conditions, point light sources at different viewing angles replicate nighttime glare scenarios such as oncoming headlights. Both types of glare result in reduced visual acuity and increased discomfort beyond a certain illuminance threshold. Because photosensitive individuals are often unlicensed drivers and experience the greatest impairment during daylight hours, we recommend using a uniform light source to assess their daily visual function. In contrast, nighttime driving ability should continue to be assessed using point light sources. With the advent of coherent laser light sources in automotive headlights [40] and the widespread use of pulse width modulation (PWM) for brightness control in LED headlights [41], glare characteristics are evolving [42]. Coherent laser light sources can produce highly collimated beams, potentially increasing the intensity and sharpness of glare effects, while PWM modulation introduces flicker, which may further contribute to visual discomfort, particularly in photosensitive individuals [43]. Future studies should take these technological advances into account when evaluating glare effects. In addition, point light sources should be placed more centrally than the 23.5° and 13.3° eccentricities used in this study to ensure an adequate glare effect under test conditions.

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