Chromatic discrimination in young carriers of red-green colour vision deficiencies

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Abstract

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Purpose: Visual discrimination skills, like discrimination of motion and colour, improve throughout adolescence in normal trichromats. Some adult carriers of red-green colour vision deficiencies exhibit reduced colour discrimination, but little is known about colour discrimination abilities in young carriers. The aim of this study was to assess the colour discrimination abilities of young obligatory carriers.

Methods: 100 normal trichromatic females (aged 18.28 (±7.11) years) and 30 obligatory carriers of red-green colour vision deficiencies (8 protan carriers and 22 deutan carriers, aged 32.07 (±15.5) years) were tested with a battery of colour vision tests comprising Ishihara (24 pl. ed.), Hardy-Rand-Rittler 4thed. (HRR 2002), Neitz Test of Color Vision (NTCV), Cambridge Colour Test (CCT), Farnsworth-100-Hue Test (FM100-Hue), HMC anomaloscope (both Rayleigh and Moreland matches) and Medmont C-100. The results are presented for four different age groups (9-12, 18-29, 30-39 and 40+).

Results: Carriers aged 9-12 years failed the pseudoisochromatic (PIC) tests more often than their normal trichromatic peers. These tests were failed by 80% of deutan carriers and 50% of protan carriers, but only 20% of normal trichromats in the same age group. These figures decreased to 75%, 20% and 12%, respectively, in the 30-39 year age group. Colour discrimination, as assessed by the FM100-Hue test, improved with age for both groups, but the carriers' performance was, on average, poorer than that of normal trichromats. Variability in the FM100-Hue error scores was significantly greater for the 9-12 year age group, compared to the three older age groups, both for normal trichromats and for carriers. Protan carriers required, on average, more red and deutan carriers required more green, compared to normal trichromatic females, when tested on the Rayleigh match and the Medmont C-100 tests. However, the Medmont C-100 failed to identify protan and deutan carriers amongst the normal trichromats and the null-point settings of all three groups overlapped considerably.

Conclusion: The results imply that some young female carriers may have exacerbated problems with colour discrimination due to the combined effects of being a carrier and having an immature visual system. The improvement in colour discrimination with age seen in normal trichromats is also evident in carriers of red-green colour vision deficiencies. Deutan carriers scored significantly worse on the colour vision tests used, which shows that they have poorer colour vision than protan carriers. The results from the Rayleigh anomaloscope and the Medmont C-100 tests imply that it may be possible to classify known obligate carriers as either protan or deutan carriers.

Keywords: Colour vision, Heterozygote, Visual development, Colour vision testing

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List of abbreviations

ANOVA	One-Way Analysis of Variance
CCT	The Cambridge Colour Test
CIE	The Commission Internationale de l'Éclairage
FM100-Hue	The Farnsworth 100 Hue Test
HRR 2002	The Richmond Products Hardy-Rand-Rittler 2002
KC	Koniocellular
LGN	Lateral geniculate nucleus
L-	Long
M-	Medium
MC	Magnocellular
NTCV	The Neitz Test of Color Vision
PC	Parvocellular
PIC	Pseudoisochromatic
REK	Regional Committee for Medical Research Ethics
RPE	Retinal pigment epithelium
S-	Short
SD	Standard deviation
SHDIR	The Norwegian Directorate of Health
SQRT	Square root
TES	Total error score

1 Introduction

1.1 Colour vision

Colours are everywhere: in nature, school books, magazines, the fruit counter etc. We use colours to orientate ourselves in the traffic and to differentiate football players on opposing teams. Colours tell you if the food is well prepared and if the tomato is ripe. Hence, they are an extremely important component of the information that we gather with our eyes.

Normal human colour vision is trichromatic because it depends on three different photoreceptors with overlapping sensitivities: S-, M- and L-cones, that are maximally sensitive to light at 420, ~530 and ~560 nm (Schnapf et al., 1987). The perception of colour is enabled by the ability of neural circuitry to compare light by these three classes of cone photoreceptors (Solomon and Lennie, 2007). Trichromatic colour vision is not enjoyed by all; it is possible to be either partially or entirely colour blind (Sharpe et al., 1999). The most common forms of colour deficiencies are inherited and arise from alterations in the genes that encode opsin molecules. Phenotypically, the gene alterations results in either anomalous trichromacy, dichromacy or monochromacy (Sharpe et al., 1999). Red-green colour vision deficiencies are the most common.

Due to the fact that the genes encoding the L- and M-cone photopigments are located on the X-chromosome, red-green colour vision deficiencies are a sex-linked trait. If a girl is either the mother or daughter of a red-green colour vision deficient male, she is an obligatory carrier of the gene encoding for this deficiency (Sharpe et al., 1999). Each time a heterozygotic carrier gives birth to a son there is a 50% chance that she has handed down an X-chromosome carrying the abnormal opsin gene array (Sharpe et al., 1999, Krill, 1969, Jordan and Mollon, 1997). Approximately 15% of women are heterozygote carriers of X-linked red-green colour vision deficiencies (for calculation see Ref. Waaler, 1927).

Early detection of people with impaired colour vision is advantageous, since it allows teachers to be better informed and more aware of the need for educational aids. Early detection also promotes compensation processes and adaption to the dysfunction (Marré et al., 1989). Colour defective people may experience problems when colour is used to organise a visual display, or when it is an attribute of the target object they are searching for (Cole, 2004). Since the retina of a female carrier of X-linked red-green colour vision

deficiencies consists of a mosaic of both normal and defective patches (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964), the carrier may show a slight or moderate reduction in colour vision (Feig and Ropers, 1978). Carriers may partly share their sons/fathers colour deficiency (Rodríguez-Carmona et al., 2008, Krill and Schneiderman, 1964), hence, some exhibit mild abnormalities of colour discrimination and matching (Jordan and Mollon, 1993b, Waaler, 1927). Even though a proportion of adult carriers of red-green colour deficiencies exhibit reduced red-green colour discrimination (Jordan and Mollon, 1993b), little is known about the colour discrimination abilities of young carriers. Female carriers are of interest due to their possible impaired colour vision.

1.2 Retinal anatomy and physiology - overview

The retina is a thin sheet of brain tissue, 100 to 250µm thick (Chalupa and Werner, 2004a, Standring, 2009) that covers approximately two thirds of the rear of the eye and comprises several cell layers. Histologically, from outermost to innermost, the retina consists of the following ten layers: pigment epithelium, photoreceptor outer and inner segment layers, external limiting membrane, outer nuclear layer, outer plexiform layer, inner nuclear layer, inner plexiform layer, nerve fibre layer and internal limiting membrane (for review see Ref. Standring, 2009). This classical ten-layered organisation differs in the fovea, where the five innermost layers are absent (Standring, 2009).

Light enters the visual system through the eye's pupil and strikes the very back of the retina. Light energy is then converted into neural activity through the conversion of photons into a suitable cellular event, namely a change in the membrane resistance. The information is then passed to the brain through a series of neurons (Sharma and Ehinger, 2003).

Colour vision can be defined as the sensation that allows us to discriminate uniform surfaces of equal brightness and starts with the absorption of photons in the retinal cone photoreceptors. The photoreceptors transduce electromagnetic energy into electrical voltages, which are furthermore transformed into action potentials by a complicated network of cells in the retina (Gegenfurtner and Kiper, 2003). Light passes through the ganglion layer, which is transparent, to reach the photoreceptors. The photoreceptors convey visual information to the ganglion cells through the bipolar cells. The signal is

created by synaptic interactions among bipolar, amacrine and ganglion cells (Masland, 1996) and then sent to the lateral geniculate nucleus (LGN) in the thalamus (Gegenfurtner and Kiper, 2003). Horizontal cells allow lateral connection between the photoreceptors, while amacrine cells allow lateral connections between bipolar and ganglion cells. After LGN, the information is sent to specialized cells in primary visual cortex, which is the first cortical stage of visual processing (Solomon and Lennie, 2007). The optic nerve is formed by the axons of all the ganglion cells.

1.2.1 Outer and inner segment layers of the photoreceptors

The outer and inner segment layers of the photoreceptors are made up of the outer and inner segments of the rods and cones. The photoreceptor cell bodies are located in the outer nuclear layer. The layer is thickest (approximately 50 µm) in the foveal region and contains ten rows of cone nuclei (Sharma and Ehinger, 2003). The photoreceptors convert light into nerve signals via a process called photo transduction. The distal parts of the photoreceptors are adapted for capturing the light, while the proximal parts transmit it. The outer and inner segments of the photoreceptor cells are located between the retinal pigment epithelium (RPE) and the external limiting membrane. A narrow connecting stalk separates the inner segment from the outer (Sharma and Ehinger, 2003).

There are two main types of photoreceptors: rods and cones. Cones are found in greatest concentration in the fovea and are the receptor cells used for colour vision and high visual acuity under light-adapted conditions (photopic light levels). In contrast, the rods are used in dim light (scotopic light levels) and dominate the periphery of the visual field. Rods are always smaller than cones, regardless of retinal location (Curcio et al., 1990). Peripheral to the foveola, the rods form incomplete rings around individual cones.

Although there is significant inter-individual variation in photoreceptor density (Curcio et al., 1990), the retina consists of about 4.6 to 6.5 million cones and 92 to 125 million rods (Standring, 2009, Roorda et al., 2001, Deeb, 2006). The peak cone density is 199,000 per mm^2 at the foveal centre of the average retina (Curcio et al., 1990). Cone density is 40 to 45% higher in the nasal part of retina compared to the temporal part. Furthermore, with increasing eccentricity the cone density falls steeply (Curcio et al., 1990). Near the human fovea, the arrangement of S-, M- and L-cones can be considered to be randomly organized

(Roorda et al., 2001, Deeb, 2006), implying cell migration during development (Hendrickson and Yuodelis, 1984). The central 100µm of the fovea, where visual acuity and cone density are highest, consists of only L- and M-cones (Gegenfurtner and Kiper, 2003, Curcio et al., 1990) and is blue-blind, this is known as foveal tritanopia (Curcio et al., 1991). S-cones are arranged randomly in the retina and they are sparse (approximately 10% of all cones) (Curcio et al., 1991).

The pigment molecules responsible for capturing light in the rod outer segments are called rhodopsin. The rhodopsin consists of a vitamin A derivate (11-*cis*-retinal), and is made from 349 amino acids. Cones also contain the chromophore 11-*cis*-retinal, but this opsin differs from that found in rods (Sharma and Ehinger, 2003). The cone photopigments are therefore maximally sensitive to short, medium and long wavelengths. The photoreceptor outer segments are temporarily damaged by light absorption and the proteins and other cellular components have to be replaced. The substance of the outer segments of cones is replaced every evening, whereas for rods this occurs every morning (Sharma and Ehinger, 2003).

1.3 Retinal pathways

Three major pathways convey photoreceptor signals to the brain: the parvocellular (PC), koniocellular (KC) and magnocellular (MC) pathways. All three arise from the layers of the lateral geniculate nucleus. These pathways consist of groups of cells which pass signals from the photoreceptors to the lateral geniculate nucleus, via bipolar and ganglion cells, terminating in the visual cortex, V1 (Solomon and Lennie, 2007). The PC pathway is responsive to changes in luminance and together with the MC pathway, it mediates spectral opponency of M- and L-cones. The KC pathway mediates spectral opponency of S-cones and combined inputs from S-, M- and L-cones (Chalupa and Werner, 2004b).

The cone photoreceptor pathways are concerned with both colour- and detail vision. The three different types of cone cells (S-, M- and L-cone) can induce two types of responses in bipolar cells - hyperpolarization and depolarization (both ON- and OFF-responses). The cone photoreceptor cells contact bipolar cells, which contact ganglion cells, forming a three-neuron chain through the retina (Solomon and Lennie, 2007).

In the PC pathway, midget ganglion cells oppose signals of L- and M-cones. The inputs from the L- and M-cones do generally have opposite signs. There are many more PC-cells than necessary to support colour vision and indeed, the PC pathway is also essential for spatial vision. The PC-cells in the central retina derive input from only one cone, whereas more peripherally, the PC-cells draw inputs from several cones (Solomon and Lennie, 2007).

The KC pathway carries signals from the S-cones. A specialized bipolar cell provides S-ON responses to subsequent visual processes. An S-OFF response also exists, but the source of OFF S-cone signals in ganglion cells remains unclear. S-cones do not support high visual acuity, due to their sparse distribution, hence it is likely that the S-cone pathway was evolved to provide colour vision in a dichromatic ancestor of the mammals (Solomon and Lennie, 2007).

In the rod photoreceptor pathways, approximately 75,000 rod photoreceptors drive 5,000 rod bipolar cells and 250 amacrine cells. They then converge to a single large ganglion cell. Only a single type of bipolar cell connects with rod photoreceptors and responses are always of the ON-centre depolarizing type. The rod photoreceptor pathways form a four-neuron chain through the retina and are concerned with scotopic vision. Night blindness is characterized by a loss of scotopic vision and is one of the earliest symptoms that become apparent in children with retinitis pigmentosa (Sharma and Ehinger, 2003).

1.4 Normal and deficient colour vision

1.4.1 Trichromatic colour vision

Colours play an important role in visual memory and facilitate object perception and recognition (Gegenfurtner and Kiper, 2003). Colour vision is the ability to distinguish objects based on spectral reflectance variations (Chalupa and Werner, 2004b). It is said that colour vision is based on three requirements: surfaces must show variation in spectral reflectance, photoreceptors must generate differential responses to light reflected from the surfaces and finally, post-receptoral processes must compare signals from the photoreceptors and generate codes that permit understanding of spectral differences in the environment (Chalupa and Werner, 2004b).

All colours can be matched by just three parameters - either by the three additive primary colours (violet, green and red) or by mixing the three subtractive primaries (cyan, magenta and yellow) (for review see Ref. Sharpe et al., 1999). Normal human colour vision is trichromatic, because it depends on three types of light activated pigments with overlapping sensitivities in the retina. Hence, it requires three primary colours to match all others. Circa 1800, Thomas Young put forward the hypothesis that trichromatic colour vision is a result of three different light sensitive mechanisms in the human retina (Nathans et al., 1986a). Today, we know these mechanisms as the three different photoreceptor cells (cones) in the human retina (Nathans et al., 1986a, Neitz and Neitz, 2000).

Trichromatic vision requires three different cone pigments from each of the three different, well-separated spectral cone classes (Neitz and Neitz, 2000, Sharpe et al., 1999, Nathans et al., 1986a). The three pigments are often referred to as blue, green and red. This is slightly misleading, instead the terms short-, middle- and long wavelength sensitive pigments (abbreviated S, M and L) should be used (Neitz and Neitz, 2000). Colour vision is the ability to discriminate wavelength and each of the cone pigments has their wavelengths of maximum absorbance (λ_{max}) in different parts of the visible spectrum. These are, respectively, 420 (violet), ~530 (green) and ~560 nm (yellow-green) (Schnapf et al., 1987). However, their absorption spectra overlap considerably (Sharpe et al., 1999, Merbs and Nathans, 1992, Neitz and Neitz, 2000), hence, their tuning is sufficiently broad for them to respond to light throughout the entire visible spectrum, which spans wavelengths of ~400-700 nm (Solomon and Lennie, 2007).

The ability to discriminate colour depends on the distinction in spectral sensitivity between the different pigments. The greater the distinction in spectral sensitivity, the better the ability to discriminate colour is (within certain limits) (Asenjo et al., 1994, Neitz and Neitz, 2000). Just 7 amino acid residues are responsible for the entire spectral difference of the red and green colour vision pigments (Asejno et al., 1994). People with trichromatic colour vision can distinguish more than 100 different hues in addition to black, white and grey (Neitz and Neitz, 2000).

Trichromacy is considered to be an adaption to searching for yellow and orange fruits amongst green foliage (Hunt et al., 1998, Dulai et al., 1999) and is dependent on two genes, an autosomal S-cone gene and a polymorphic X-linked M- and L-gene (Hunt et al., 1998). A

relatively recent duplication from a single ancestral gene, unequal recombination events between the two genes, may be the reason for the close homology between the M- and L-genes (Hunt et al., 1998, Nathans et al., 1986a, Nathans et al., 1986b). It has been suggested (Hunt et al., 1998) that the evolution of the spectral shift between the visual pigments encoded by these two genes occurred after duplication. The spectral differences between M- and L-cones are encoded by exons 2 to 5, of which the largest spectral shifts are encoded by changes in exon 5 (Neitz et al., 1996). The red and green pigment genes have exceptionally similar DNA sequences, showing about 98% identity and are, therefore, highly homologous (Nathans et al., 1986b, Nathans et al., 1986a). Among males with normal colour vision, the L to M ratio can vary considerably, from 1:1 to 16:1 (Hofer et al., 2005), which might be expected to influence colour vision, but in fact does not (Solomon and Lennie, 2007).

1.4.2 Polymorphism, normal trichromatic vision

The apoproteins of M- and L-cones are encoded by genes on the X-chromosome. Colour vision and colour matches among males with normal trichromatic colour vision will vary (Winderickx et al., 1992, Deeb, 2006), due to small variations in the absorption maxima of visual pigments (Winderickx et al., 1992). This may be explained by the common single amino-acid polymorphism (Ser and Ala) at residue 180 of the X-linked L-pigment (Winderickx et al., 1992, Deeb, 2006). Higher sensitivity to red light is correlated with the presence of Ser (Winderickx et al., 1992, Sharpe et al., 1999). This polymorphism on the L-pigment gives different absorption maxima for the expressed L-pigments with either Ser or Ala (Merbs and Nathans, 1992, Neitz and Neitz, 2000, Deeb, 2006). The polymorphism is not equally distributed; among L-cone pigment genes approximately 56.3 - 62% have Ser and 38 - 43.7% have Ala (Sharpe et al., 1999, Winderickx et al., 1992).

For two polymorphic variants of the L-pigment, the mean values for the wavelength of maximal absorption are 552 and 557 nm, respectively. Rayleigh matches made by males with normal colour vision may have a bimodal distribution, due to this polymorphism, with a variation in red pigment absorption of several nanometres (Merbs and Nathans, 1992). Because of the polymorphism that occurs at codon 180, the presence of Ser or Ala results in a shift to shorter or longer wavelengths (Sharpe et al., 1998, Merbs and Nathans, 1992,

Asejno et al., 1994), respectively, of ~ 4 nm (Merbs and Nathans, 1992) or 2-7 nm (Asejno et al., 1994).

The M-pigment is also highly polymorphic (Winderickx et al., 1992, Neitz and Neitz, 2000, Sharpe et al., 1999, Deeb, 2006). Among M-cone pigment genes, approximately 6% have Ser and 94% have Ala (Sharpe et al., 1999). This polymorphism may have resulted from the shuffling of the L- and M-gene segments which has occurred in the process of human evolution (Neitz and Neitz, 2000, Jacobs and Deegan II, 2003).

1.4.3 Colour vision deficiencies

Red-green colour vision deficiencies usually arise from unequal crossing-over between the red and green pigment genes (Drummond-Borg et al., 1988, Nathans et al., 1986a). This leads either to hybrid (fusion) genes, consisting of both red and green pigment genes, or to pigment gene deletions (Drummond-Borg et al., 1988). Colour deficient subjects confuse colours that normal trichromats can easily distinguish. The term “colour confusion” describes a subject mistaking one primary colour for another, whereas the term ”poor colour discrimination” describes less extreme mistakes (Kainz et al., 1998).

The highest rates of X-linked colour deficiencies are found in Europeans and the Brahmins of India, whereas the lowest incidences occur in Brazil, the South Pacific Islands, North America and in the Aboriginal population of Australia (Sharpe et al., 1999).

1.4.4 Anomalous trichromacy

There are two different types of anomalous trichromacy, namely protanomaly and deuteranomaly; both arise from the loss of one class of cone photopigment. Just like dichromats, anomalous trichromats are missing one normal cone pigment. They still possess trichromatic colour vision, but it is not based on S-, M and L-pigments, as it is in those with normal colour vision. An anomalous trichromat will have two normal cone pigments and, in addition, an abnormal or anomalous cone pigment differing by a small shift in spectral peak (Neitz and Neitz, 2000) or along the wavelength axis (Deeb et al., 1992). The abnormal M- and L-cone pigments are M-L chimeras, encoded by hybrid genes (Deeb, 2006). Either of two polymorphic versions of the normal pigment can be paired with any one of many green-like or red-like anomalous pigments, resulting in a change in

spectral sensitivity of both the normal and anomalous pigment shift. This can be detected by a shift in the midpoint of the Rayleigh match on an anomaloscope (Sharpe et al., 1998).

Protanomalous trichromats have one S-pigment and two M-pigments, while deuteranomalous trichromats have one S-pigment and two L-pigments. The two M- or L-like pigments differ by a small shift in spectral peak. People diagnosed as anomalous trichromats can have colour vision that ranges from nearly dichromatic to nearly normal (Sharpe et al., 1999, Neitz and Neitz, 2000), categorized as “extreme” or “simple”, respectively (Sharpe et al., 1999). Anomalous trichromats in the extreme category may have nearly as poor colour vision as dichromats, whilst those in the simple category may have almost normal colour vision and, furthermore, may be unaware of their deficiency (Sharpe et al., 1999). This is explained by the difference in spectral peak between the two abnormal cone pigments (Neitz and Neitz, 2000). As the separation between the spectral sensitivities of the anomalous and the normal pigments decreases or increases, the poorer or better the chromatic discrimination will be (Sharpe et al., 1998). For instance, a deuteranomalous person with a large spectral difference between the L-pigment subtypes would have the basis for better colour vision than a person where the two L-pigment subtypes are nearly identical (Neitz and Neitz, 2000). For anomalous trichromats, distinguishing between pastel shades is more difficult than distinguishing between well saturated versions of the same colours. For instance, they may be able to distinguish between red and green, but not between more similar colours such as olive green and brown (Neitz and Neitz, 2000). The anomalous hue locations are shifted to shorter wavelengths for protanomalous trichromats and longer wavelengths for deuteranomalous trichromats and unlike dichromats, they can see more than two hues in the spectrum (Sharpe et al., 1999).

Deuteranomaly

Deuteranomaly is the most common type of all inherited colour vision deficiencies (Sharpe et al., 1999, Neitz et al., 1996) and affects about 4.61% of the Caucasian males. In the Caucasian female population, the incidence of deuteranomaly is about 0.36% (Sharpe et al., 1999). Deuteranomaly is based on three pigments: one S-cone and two spectral subtypes of L-cones. This means that people with deuteranomaly have at least two different genes to encode L-pigments (Neitz and Neitz, 2000, Neitz et al., 1996); hence they have more L-than

M-genes and have many more L-genes than are found in normal trichromatic men (Neitz and Neitz, 2000), who generally have more M- than L-genes.

Protanomaly

Protanomalous trichromats have lost all their L-pigments. They possess two M-pigments, which differ by a small shift in spectral peak and one S-pigment (Neitz and Neitz, 2000). Protanomaly affects about 1.07% of the Caucasian males, and in the Caucasian female population, the incidence is about 0.03% (Sharpe et al., 1999).

1.4.5 Dichromacy

Dichromacy is the most severe of the common inherited red-green colour vision deficiencies. A dichromat's colour vision is based on just two cone pigments (Neitz and Neitz, 2000, Sharpe et al., 1999) and it is therefore two dimensional (Sharpe et al., 1999). The direct cause of colour vision loss in dichromacy is, in most cases, the loss of the genes that encode one class of cone photopigment, a straightforward deletion of cone pigment genes. In some rare cases, the dichromacy can be explained by a genetic defect, associated with one intact cone pigment, which interferes with the expression or function of the encoded cone pigment. This problem might arise from an as yet unidentified deleterious mutation that interrupts photopigment expression or function. Dichromats can be divided into three groups: protanopia, deuteranopia and tritanopia. Protanopes have lost L-pigments, deuteranopes have lost M-pigments and tritanopes have lost S-pigments (Neitz and Neitz, 2000).

Most red-green dichromats confuse red with green; they also confuse colours in the spectrum that fall between red and green, such as yellow, orange and brown (Neitz and Neitz, 2000). Only a slight difference in the wavelength of their neutral points distinguishes protans from deutans, 493 nm and 497 nm, respectively. While protanopes confuse blue-green with red, deuteranopes confuse blue-green with purple (Lakowski, 1969a). Dichromats require only two primaries to match all colour stimuli, while normal trichromats require three. This means that dichromats confuse or fail to discriminate colours that are easily distinguished by normal trichromats. Protanopes can distinguish only about 21 distinct wavelengths and deuteranopes can distinguish 31, whereas normal trichromats

discriminate about 150 wavelengths in the spectrum. Normal trichromats see at least seven pure hues (red, orange, yellow, green, cyan, blue and violet), while the dichromat's spectrum consist of just two pure hues (Sharpe et al., 1999). Protanopes and deuteranopes distinguish colours between yellowish-green and red on the basis of saturation and lightness. The major difference between protanopes and deuteranopes is that red appears relatively darker in the protanopic simulation than in the deuteranopic one (Sharpe et al., 1999). The incidence of protanopia and deuteranopia is approximately equal in the Caucasian male population (1.01% and 1.28%, respectively) (Sharpe et al., 1999). In the Caucasian female population, the incidence of protanopia and deuteranopia is lower (0.02% and 0.01%, respectively) (Sharpe et al., 1999).

Some protanopes have arrays consisting of a hybrid gene that encodes a pigment with similar spectral sensitivity to that of the normal green pigment and, in addition, one or more normal green pigments. Some deuteranopes have arrays consisting of a normal red pigment and a hybrid gene that encodes a pigment similar to that of the normal red pigment (Sharpe et al., 1998, Nathans et al., 1986a, Deeb et al., 1992). Some deuteranopes may reject colour matches made by other deuteranopes (Merbs and Nathans, 1992). This is thought to be due to polymorphism in the L-pigment, where the absorption maxima differ subtly from the others in its spectral position (Merbs and Nathans, 1992, Deeb, 2006).

Tritan deficiencies, which affect the S-cones, are often referred to as blue-green disorders (Sharpe et al., 1999). Like protan and deutan deficiencies, tritanopia arises from alterations in the gene encoding the opsin. Unlike protan and deutan deficiencies, tritanopia is autosomal in nature, linked to chromosome 7 (Sharpe et al., 1999, Baraas et al., 2007). Because of its incomplete penetrance, individuals with the same underlying mutation can manifest different degrees of colour vision impairment (Baraas et al., 2007). This type of deficiency affects the ability to discriminate colours in the short- and middle wave regions of the spectrum (Sharpe et al., 1999). It has been suggested that tritan deficiencies are progressive S-cone dystrophies, with a disruption in the regularity of the cone mosaic (Baraas et al., 2007). It has been proposed (Pokorny et al., 1981) that although the majority of tritans have functioning S-cones, their number and/or distribution pattern is abnormal. Tritan deficiencies are very rare - the incidence of the deficiency in the United Kingdom has been estimated as 1:13,000 to 1:65,000 (Sharpe et al., 1999).

1.4.6 Monochromacy

Subjects who have lost the function of all three cone types are referred to as rod monochromats, or are described as having complete achromatopsia (Sharpe et al., 1999). Blue-cone monochromacy is caused by the loss or rearrangement of the X-linked opsin gene array, resulting in only rods and S-cones functioning correctly (Sharpe et al., 1999). In a third type of cone monochromacy, it is assumed that subjects have either M- or L-cones. In this case the S-cones are assumed to be totally absent or inactive, but may actually be partially functioning. People with either rod- or blue-cone monochromacy have poor vision and nystagmus; in contrast, those with M- or L-cone monochromacy have normal visual acuity. However, few cases of M- and L-cone monochromacy have ever been described and none is fully accepted as authentic (Sharpe et al., 1999).

1.5 Inheritance patterns of red-green colour vision deficiencies

Every human cell has 46 chromosomes (with the exception of sperm and ova, which have 23). Of these 46 chromosomes, 44 are called autosomes and can be grouped in 22 identical partner pairs. With one exception, the pairs are the same in males and females. The pair that is not identical contains the sex chromosomes. In women, the two sex chromosomes are similar and are referred to as X-chromosomes. In men, the sex chromosome pair comprises one X-chromosome and one unique Y-chromosome. The Y-chromosome is male-determining. If a trait is determined by a gene carried on one of the X-chromosomes, it is called sex- or X-linked (Krill, 1969).

The genes encoding the M- and L-pigments lie on the X chromosome (Sharpe et al., 1999, Solomon and Lennie, 2007) and are arranged in a head-to-tail tandem array at Xq28 (Deeb, 2006). These genes are inherited as X-linked recessive traits, which explain the difference in the frequency of red-green deficiencies between the sexes (Neitz and Neitz, 2000, Sharpe et al., 1999). Since males have only one X-chromosome, they are homozygous and will always manifest a colour deficiency if they inherit an aberrant gene (Sharpe et al., 1999). Females have two X-chromosomes, one inherited from each parent and they will usually not show a complete manifestation of typical colour vision deficiencies unless they are homozygous (Sharpe et al., 1999). Father-to-son transmission of red-green deficiencies is

not possible, since they are X-linked. The inheritance pattern of the X-linked red-green colour vision deficiency is shown schematically in Figure 1-1.

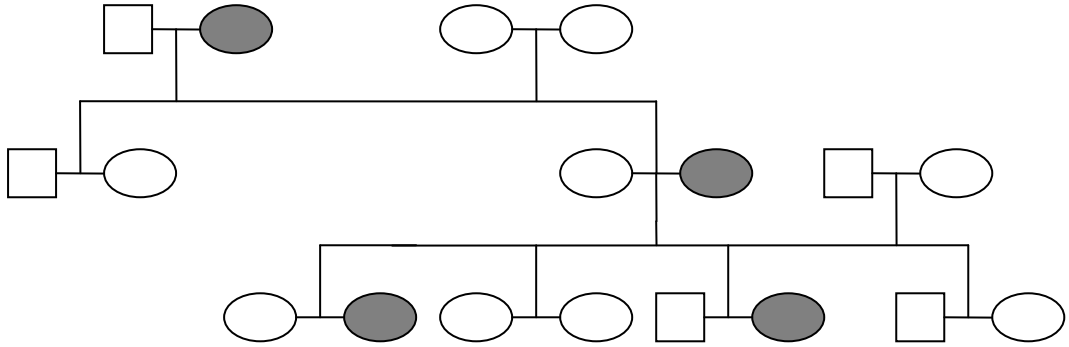

Figure 1-1 Inheritance pattern of the X-linked red-green colour vision deficiency. The square represents the Y-chromosome, the circle represents the X-chromosome and the grey circle represents the X-chromosome with an aberrant gene.

1.6 Female carriers of X-linked red-green colour vision deficiencies

1.6.1 Superior colour vision?

It is often said that women are more discriminating than men in the use of colour names and that they access a larger repertoire of words to describe sets of colour stimuli (Rodríguez-Carmona et al., 2008). This is often taken to imply superior colour vision. Recent studies have refuted this hypothesis, concluding that women do not have superior red-green colour discrimination (Rodríguez-Carmona et al., 2008, Pardo et al., 2007). In fact, one of the studies implied that woman may, on average, have poorer discrimination than men (Rodríguez-Carmona et al., 2008), and that men and women cannot be considered to form a homogenous population (Pardo et al., 2007)

1.6.2 Heterozygote and homozygote carriers

If a female is homozygous, the gene is present on both of her two X-chromosomes (Krill, 1969). Subjects with two different variants of a gene, for instance one recessive and one dominant, are called heterozygote. They carry an abnormal opsin gene array from one

parent and an X-chromosome carrying a normal opsin gene array from the other (Sharpe et al., 1999, Krill, 1969). According to classical theory, female heterozygous carriers of red green colour vision deficiencies should show no manifestations of the defect, due to the recessive behaviour of the defective gene of one X-chromosome (Krill, 1969, Waaler, 1973). About 47% of females are heterozygotes (Winderickx et al., 1992), and approximately 15% of women are heterozygote carriers of X-linked red-green colour vision deficiencies (see 1.1.) and possess a genetic abnormality on one of their two X-chromosomes (Bimler and Kirkland, 2009). This means that every sixth or seventh female will be a carrier (Waaler, 1973). Of Caucasian heterozygous females, about 4.5% are carriers of either protanopia or deuteranopia, and about 11% are carriers of anomalous trichromacy (Sharpe et al., 1999). Whilst heterozygote females are carriers of the deficiency, homozygote females are presumably colour deficient.

A heterozygote carrier will pass on an X-chromosome carrying an abnormal opsin gene array to half of her sons and half of her daughters (Sharpe et al., 1999, Krill, 1969, Jordan and Mollon, 1997). Sons of heterozygote carriers have a 50% risk of colour deficiencies, whilst sons of homozygotes have a 100% risk (Feig and Ropers, 1978).

1.6.3 Obligatory and compound carriers

If a girl is either the mother or daughter of a red-green colour vision deficient male, she is an obligatory carrier of the gene encoding for this deficiency (Harris and Cole, 2005b, Kainz et al., 1998, Krill, 1969). If a girl is a carrier for two different colour deficiencies (both X-chromosomes contain genes encoding for different deficiencies), for example, both protanopia and mild deuteranopia, she is a compound heterozygous carrier, also known as a double carrier. These girls, with a protan deficiency on one X-chromosome and a deutan deficiency on the other, usually have normal colour vision (Drummond-Borg et al., 1988, Tait and Carroll, 2009).

1.6.4 X-chromosome inactivation and mosaic pattern

A female carrier has a different form (allele) of either M- or L-gene on each X-chromosome (Hunt et al., 1998). Which X-chromosome that will be expressed on in a given cone cell is determined by a random X-chromosome inactivation (Lyon, 1972). This ensures that only one allele is expressed per photoreceptor (Hunt et al., 1998). Due to this X-chromosome

inactivation and the random distribution of cones in the central human retina, patching would be expected in heterozygous female carriers of colour vision deficiencies (Deeb, 2006). This produces a mosaic pattern on the retina, with subsets of cones that express both the abnormal and the normal chromosome, respectively. The abnormal chromosome will be inherited by the female carrier's colour deficient son. Through modern genetic testing, it has been shown that the X-inactivation is related to methylation on the activated X-chromosome and unmethylation on the inactivated chromosome (Jørgensen et al., 1992).

Heterozygote carriers will exhibit retinal patches with either Ser or Ala at position 180 of the L-pigment. This X-linked polymorphism may be explained by the X-inactivation in females. The Ser/Ala polymorphism is therefore highly correlated with the major differences in Rayleigh matches on the Anomaloscope. Female carriers would show intermediate match midpoints (Winderickx et al., 1992).

Since the carrier's retina probably consists of a mosaic of normal and defective patches (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964), the presence of green and red cones with normal pigments makes for normal colour vision (Drummond-Borg et al., 1988). The carrier's retina mosaic can vary from predominantly normal to predominantly defective, due to the random nature of the X-inactivation (Lang and Good, 2001). In a heterozygote carrier, the normal patches are expected to be sufficient to support normal colour discrimination and hue perception (Miyahara et al., 1998).

The process of random X-inactivation implies that for female heterozygote carriers of deutan deficiencies, about 50% of green cones will carry the abnormal gene array and 50% will carry the normal green gene. For protan carriers the same is true for the red gene arrays (Drummond-Borg et al., 1988). This means that carriers of anomalous trichromacy will have four types of cones in their retina: the three normal types and the anomalous type that their sons may inherit (Jordan and Mollon, 1993b, Pardo et al., 2007, Sharpe et al., 1999, Kainz et al., 1998). A deuteranomalous carrier's retina will therefore contain normal long wavelength sensitive photopigments and areas of normal medium wavelength sensitive photopigments. These patches will be intermixed with patches of deuteranomalous middle wavelength photopigments, showing that carriers can possess more than three types of photopigments (Lang and Good, 2001). It has been hypothesized that such women have tetrachromatic colour vision, i.e. they have an extra dimension of

colour discrimination and thereby gain an advantage, rather than a disadvantage, from the mosaic character of their retina (Jordan and Mollon, 1993b, Pardo et al., 2007, Sharpe et al., 1999). A tetrachromat will need four variables to match all colours in a classical colour-matching task (Jordan and Mollon, 1993b). The existence of tetrachromatic colour vision is, however, disputed (Jordan and Mollon, 1993b).

1.6.5 The female carriers L and M-cone ratio

Based on a protan carrier's phenotype and genotype, she is expected to have a low L to M ratio, often of about 0.5:1.0 (Hofer et al., 2005). Because of this greatly under-represented L-cone class (Roorda and Williams, 1999, Miyahara et al., 1998), it is assumed that heterozygote carriers may misjudge the colour appearance of tiny objects (Roorda and Williams, 1999). In normal subjects, the average ratio of L to M-cones is close to 2:1 (Hood et al., 2006); a consequence of this is that a deutan deficiency carrier will have a particularly high proportion of L to M-cones in her retina (Hood et al., 2006, Hayashi et al., 2001, Miyahara et al., 1998). One of her X-chromosomes will lack an expressed gene for an M-cone photopigment and on average, this X-chromosome will be active in only half of her retinal cones (Hood et al., 2006, Hayashi et al., 2001). These cones will be obligatory L-cones and her overall L to M-cone ratio will have an expected value of 5:1, instead of the normal 2:1 (Hood et al., 2006). This extreme L to M-cone ratio is present in deutan, but not in protan carriers. Some claim that it impairs colour discrimination (Hood et al., 2006), while others claim that it does not (Miyahara et al., 1998). It has been reported that the more symmetrical the L to M-cone ratio, the better is the subject's chromatic contrast sensitivity (Hood et al., 2006). This implies that the colour vision of deutan carriers will be poorer than that of either protan carriers or normal observers (Hood et al., 2006).

1.6.6 Schmidt's and de Vries' sign

Compared to normal observers, protan carriers are less sensitive to red light, a characteristic known as Schmidt's sign (Schmidt, 1934, Hood et al., 2006, Jordan and Mollon, 1993b). This observation was first described mid 1930s and is attributed to the retina's mosaic pattern (Harris and Cole, 2005a). Unlike protan carriers, deutan carriers are significantly more sensitive to red light (Hood et al., 2006, Crone, 1959, Jordan and Mollon, 1997, Lang and Good, 2001) and show reduced sensitivity on the short wavelength region of the relative luminous efficiency curve (Crone, 1959). They fall well within normal limits,

with a higher than average score on the long wavelength side (Crone, 1959). This phenomenon is called de Vries' sign and is said to be more difficult to demonstrate than Schmidt's sign (De Vries, 1948, Jordan and Mollon, 1997).

1.6.7 Female carrier colour vision

Since female heterozygote carriers are believed to have cone photoreceptor ratios and cone photopigments that differ from normal (Kainz et al., 1998) and since their retinas consist of both normal and defective cones (Feig and Ropers, 1978, Sharpe et al., 1999), their ability to discriminate colours will vary from point to point on the retina (Born et al., 1976, Jordan and Mollon, 1993b, Sharpe et al., 1999). Female carriers of X-linked red-green colour vision deficiencies are expected to have normal colour vision, but about 1% of heterozygotes have gross defects of their colour vision (Feig and Ropers, 1978). It has been claimed that this frequency of colour deficient females is higher than the expected frequency of homozygotes (Feig and Ropers, 1978). Female carriers of X-linked red-green colour vision deficiencies may show a slight or moderate reduction in colour vision (Feig and Ropers, 1978) and exhibit mild abnormalities of colour discrimination and matching (Jordan and Mollon, 1993b, Waaler, 1927). Carriers may partly share their sons/fathers colour deficiency (Rodríguez-Carmona et al., 2008, Krill and Schneiderman, 1964). However, the colour deficient sons of heterozygote female carriers exhibit greater colour deficiency than their mothers (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964).

1.6.8 Deviant behaviour on colour vision tests

Not all normal trichromatic subjects "pass" all colour vision tests; neither do all those with colour vision deficiencies "fail" all colour vision tests. Similarly, although carriers are expected to have normal colour vision, they do not always pass all colour vision tests (Hill, 1980, Krill and Schneiderman, 1964).

Carriers' colour vision can be variable, resulting in them failing some tests, passing others and also scoring differently during repeated testing (Waaler, 1973). Heterozygote carriers of X-linked red-green colour vision often have slight to moderate colour deficiencies, and therefore they often fail and make more mistakes on the Ishihara test than do normal trichromatic subjects (e.g. Crone, 1959, Waaler, 1927, Jordan and Mollon, 1993b, Waaler, 1967, Hill, 1980). Bailey et al. (2004) have reported a deutan carrier that made an error on

plate seven when tested with the Richmond Products Hardy-Rand-Rittler 2002 (HRR 2002). She read the plate correctly on second administration.

It has been reported that carriers exhibit a shift in Nagel match mid-point, an enlarged Nagel matching range (Waaler, 1927, Jordan and Mollon, 1993b, Hill, 1980, Krill and Schneiderman, 1964) and impaired discrimination of saturation and hue (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964). Regan et al. (1994) have reported a protan carrier who on average exhibited ellipses on Cambridge Colour Test (CCT), Ellipse test, that were oriented at a lower angle for her than for the normal trichromatic observers, however, this difference was not significant.

Colour-space compression in a red-green dimension and reduced salience of that dimension is also often seen in heterozygous women (Bimler and Kirkland, 2009). Some studies have shown that carriers' performance is poorer when tested with the Farnsworth 100 Hue Test (FM100-Hue) compared with normal trichromatic females (Hill, 1980, Krill and Schneiderman, 1964, Verriest, 1972), while other reports that their performance does not differ from that of normal trichromatic observers (Jordan and Mollon, 1993b). The majority of both protan and deutan heterozygote carriers, however, are classified as normal by standard clinical colour vision tests (Jordan and Mollon, 1993b). It has been claimed that 15.5% of heterozygote female carriers score worse than their genotypically normal counterparts on different colour vision tests (Verriest, 1972). It is apparent that the more sensitive the tests are, the easier it is to detect carriers and other subjects with slight colour deficiencies (Krill and Schneiderman, 1964). In a study performed in the Netherlands (Marré et al., 1989), 3.66% of the girls were classified as "case in doubt" and were concluded to be false positives. Whether some, or all, of them were carriers was not discussed in the report.

1.7 Abnormal colour vision and daily life

Some people with abnormal colour vision report that they experience problems with colour at work, school and in everyday life (Tagarelli et al., 2004, Cole, 2004, Bacon, 1971). Colour coding is common, for example in traffic signals, warning lights, books, schools, sports, computers etc. In short, interpreting colours is a necessity wherever you are and whatever you are doing (Cole, 2004). Colours are used in teaching, especially at lower levels. If a child is colour deficient, the use of colours in teaching may affect his/her ability to achieve

success at school (Gordon, 1998). Good career guidance for young colour deficient people is necessary (Gordon, 1998, Cole, 2004). Furthermore, it is said that in about 30% of colour deficient people, their career choice is affected by their colour vision (Cole, 2004).

1.8 Testing girls' colour vision

Earlier colour vision studies have predominantly included only boys as test participants (Marré et al., 1989, Holroyd and Hall, 1997). Two recent reports presented results from the Neitz Test of Color Vision (NTCV) (Neitz and Neitz, 2001, Baraas, 2008), but only the latter (Baraas, 2008) included results for both males and females . Results from other colour tests have also been predominantly reported for boys, for example the HRR 2002 (Birch, 1997a, Bailey et al., 2004, Cole et al., 2006), the Ishihara test (Hill et al., 1982, Birch, 1997b, Birch, 2008) and studies that used the anomaloscope (Lloyd et al., 1984, Barbur et al., 2008, Birch, 2008). Some studies have, however, reported FM100-Hue test results for equal numbers of females and males (Verriest et al., 1982, Kinnear and Sahraie, 2002). Given this lack of data, it is difficult to define what constitutes normal or deficient colour vision in female subjects.

1.9 Childhood screening

Screening for colour vision deficiencies at an early age is important, but colour vision testing can be perceptually and cognitively challenging for children, since colour vision tests are often designed for adults (Dain and Ling, 2009, Birch, 1993). Both normal and colour deficient children tend to have higher error scores on colour vision tests, compared to adults. The older the child is, the fewer the errors or false positives answers exist (Hill et al., 1982, Lakowski, 1969a). This has been demonstrated with several colour vision tests, for example, the Ishihara and HRR 2002 (Hill et al., 1982). Some propose that children understand the concept of seriation as shown on tests with varying grey levels (Dain and Ling, 2009), and would therefore not experience problems when they are performing the FM100-Hue test. However, maturation of visual function can occur over different timescales in different children (Norcia and Manny, 2003). Screening for impaired colour vision is not part of the Norwegian Directorate of Health's recommendations for screening children's vision (SHDIR, 2009).

1.10 Former studies

In 2006/2007, 1518 females and 1445 males took part in a colour vision study. The participants were aged 6-13 years and came from primary schools in the municipalities of Kongsberg, Notodden, Bø and Tønsberg in Norway. When Tønsberg is disregarded, 959 females and 937 males took part in the study (Baraas, 2008). The NTCV-test (Neitz et al., 2001) was administrated to each child. Children who made one or more errors on the test were retested, in a separate room, with another form of NTCV and with the fourth edition of the HRR 2002 pseudoisochromatic (PIC) test for colour vision (Bailey et al., 2004, Cole et al., 2006). If the child made one or more errors on the NTCV (Neitz et al., 2001, Neitz and Neitz, 2001), or two or more errors on the HRR 2002 (Cole et al., 2006), he or she was considered to have a colour deficiency. Using these two criteria, 45 females (2.96%) and 117 males (8.09%) were classified as red-green colour deficient. When Tønsberg is disregarded, 2.82% females (n=27) and 8.43% males (n=79) were classified as red-green deficient. Compared to earlier studies, the percentage of females classified as red-green deficient was both higher than in other studies and higher than expected. This is evident both when looking at all four municipalities together, and when Tønsberg is disregarded. Because these are results from screening, it cannot be proved that these children actually have a colour vision deficiency before they have been tested further with other colour vision tests (Baraas, 2008).

1.11 CIE-diagram

CIE-diagram is a mathematical system which makes it possible to describe colour using three numbers. The CIE-diagram was first composed by the International Commission on Illumination, hence the name CIE-diagram. This system, X Y Z, embodying the primaries red, green and blue (R G B), specifies a mathematical function, which makes it possible to find the relative amounts of the three primaries that are required to match a specified colour under standard illumination. The most convenient way of showing the colour confusions of dichromats is to use the CIE chromaticity diagram. In a CIE-diagram, you can see confusion loci, centre of confusion and neutral axes for dichromats. This is shown with so-called isochromatic lines for the given dichromat. These straight lines are the dichromats confusion loci, and are systematic and directional. The direction of these lines and the position of their loci determine and distinguish different types of deficiency (Lakowski, 1969a).

2 Method

2.1 Research question and significance

2.1.1 Primary goal

Visual discrimination skills, such as discrimination of motion and colour, improve throughout adolescence in normal trichromats. Some adult carriers of red-green colour deficiency exhibit reduced colour discrimination, but little is known about colour discrimination abilities in young carriers. The aim of this study was to assess and evaluate colour discrimination abilities of young female observers, who were obligatory carriers of red-green colour vision deficiencies and to compare their results with those of adult carriers.

2.1.2 Secondary goal

Other, related, research questions were also investigated. For example, do these young carriers fail more colour vision tests than their normal trichromatic peers? Which tests do they fail? What kind of errors do they make? Are they carriers of protan or deutan deficiencies? Are they heterozygote or homozygote carriers?

Subjects of different ages were tested to determine whether there is an age effect among female carriers of colour vision deficiencies. In other words, do young carriers make more errors on colour vision tests than older carriers?

2.2 Study design

The design of this study was descriptive and analyses were based on the following variables: performance on colour vision tests, whether subjects were carriers of colour vision deficiencies or not and age. This design was used to characterize female carrier performance on various colour vision tests and also to assess colour discrimination abilities of young carriers compared to adult carriers. It was hoped that this would yield valuable information regarding childhood screening of colour vision deficiencies. To investigate whether age affects a carrier's performance on colour vision tests, different age groups were included and studied.

2.3 Study subjects

2.3.1 Recruitment

Subjects were recruited from the girls who had participated in the former studies carried out in Kongsberg, Notodden and Bø in 2006/2007 (for review see 1.10), from female optometry students at Buskerud University College and from colour deficient boys who had participated in screenings at primary schools in Kongsberg, which were carried out by the Department of Optometry and Visual Sciences, Buskerud University College in January 2008 and 2009. A questionnaire regarding familial colour vision deficiencies was sent to the girls who had participated in the 2006/2007 study. Families with fathers who had a known colour deficiency were asked whether father and daughter would participate in the study. For those who did have a colour deficient brother or maternal grandfather, their mother was asked to participate. Colour deficient boys from the study in Kongsberg in 2006 and the screening in primary schools in 2008-2009, together with their mothers, were also asked to participate in the study. All the female optometry students in 2009 at Buskerud University College were sent a questionnaire and were asked to participate.

Only known, obligate carriers were included in this study, where the status as a carrier is inferred from the status of the colour vision of her son/father.

To recruit the participants, a written consent (Appendix D) was send to each family. The written consent included the purpose of the study, its design and ethical considerations.

2.3.2 Subject samples

The subject sample was divided into three different groups:

1) During the colour vision studies in 2006/2007 in Kongsberg, Notodden and Bø, 959 girls were tested. If their fathers were colour deficient, then both father and daughter were asked to participate in the current study. For those who did have a colour deficient brother or maternal grandfather, their mother was asked to participate. The number of participants from this group was seven girls, six fathers and two mothers. An additional 39 girls, who were classified as normal trichromats without any known colour deficient relatives, participated.

2) Boys who were classified as colour deficient in the study in Kongsberg (n=37), together with their mothers, were asked to participate in the current study. Similarly, boys who were classified as colour deficient during the school screenings in Kongsberg in January 2008-2009 (n=20), together with their mothers, were asked to participate. This group comprised 15 boys and 15 mothers.
3) Female optometry students (n=205), regardless of familial colour vision history, were asked to participate in the study. This group comprised 67 women.

2.3.3 Size of sample

In total, 151 subjects participated in this study. One hundred were normal trichromatic females, eight were carriers of a protan deficiency, 22 were carriers of a deutan deficiency and 21 were colour deficient men (15 deutan deficient, six protan deficient).

2.3.4 Inclusion criteria

Subjects were either children aged 7-13 years, or adults older than 18 years. Both groups contained subjects with normal, impaired or deficient colour vision. All participants belonged to one of the sample groups described above. All were in good health, without any ocular diseases or systemic diseases affecting the eyes. Each participant read, signed and returned a written consent form prior to testing.

2.3.5 Exclusion criteria

Subjects with blindness or any other physical or psychological impairment that would prevent them from participating were excluded from the study. Subjects with ocular diseases, or with systemic diseases that affected the eyes, were excluded. Subjects who failed to sign and return the written consent form were also excluded.

2.4 Analysis and statistical issues

The raw data, collected from the questionnaire and colour vision testing, were stored in a manual paper archive and were also stored in electronic form by manually entering them into Microsoft Office Excel 2007. The names of the participants were not stored electronically, just their identification numbers. All data were controlled as regards to

biases. By looking at outliers, unrealistic values were identified and compared with the collected data and if still considered as unrealistic values, they were excluded and treated as missing data.

The data were measured and analyzed as the testing proceeded. SPSS version PASW Statistic 17.0 for Windows was used for the statistical analyses, which consisted of One-Way Analysis of Variance (ANOVA) (f) and the Student t-test (t). To prevent Type 1 errors a Bonferroni correction was carried out when three groups were compared. The level of significance was $p < 0.05$. Details of specific analyses, degrees of freedom etc, are given in the Results Chapter (3). All variables used in these analyses were derived either from the questionnaire answers, or from the results of the colour vision testing. The mean values and standard deviation of the tests are given in the Results Chapter (3).

2.5 Ethical considerations

This research was carried out in accordance with the principles embodied in the Declaration of Helsinki (Code of Ethics of the World Medical Association) and was approved by the Regional Committee for Medical Research Ethics for the Southern Norway Regional Health Authority (REK). The study dealt with personal health information and was, therefore, reported to the Data Inspectorate (Personvernombudet). In addition, personal information was stored electronically and a manual record containing sensitive personal information was created. The application to the Ethics Committee included a copy of the questionnaire, a registration list and the written consent of each participant. When reported to the Data Inspectorate, approval from REK was attached.

There was no risk or danger associated with the tests administrated in this study, nor was there any associated discomfort. Several tests were carried out and it was possible for the subjects to become tired and unmotivated, since the total test duration was between one and 2.5 hours. The anomaloscope test, in particular, could seem long and difficult. It was important, therefore, that subjects were given sufficient information prior to the study and sufficient time to carry out the tests. When needed, breaks were given between the different tests. Participants were encouraged to ask questions before, during and after testing. If the subject needed to have their vision tested, then they were encouraged to go and see an optometrist.

The written consent form (Appendix D) included general information about the project, such as its purpose and the methods to be used and outlined the practical and other consequences of participation. For children under 18 years old, parental consent was necessary. Children over 12 had to provide written consent; children under 12 did not, but it was still important that they were well informed. Participants could withdraw their consent and desist from participating at any time, without needing to give any explanation and without fear of negative consequences.

To secure the privacy of the research subjects, all personal information and data were handled confidentially. The analysed data did not contain any personal information. Each participant was allocated a unique reference number, which was stored in a database. The reference numbers were used in the statistical analyses, ensuring the anonymity of the participants and protecting their personal data. It was not possible to identify people, either directly or indirectly, through background information such as, for instance, municipality of residence or institutional affiliation, combined with data on age, sex, profession, diagnosis, etc. A list associating the participants with their reference numbers was stored separately, along with additional personal information. The electronically stored research material contained a reference number to associate it with the data stored manually. Personally identifiable information (e.g. lists of names, field notes and interview material) was stored responsibly for a limited period of time and was then deleted once it had served its original purpose.

The scoring sheets (Appendix F) used to data registration were systematized and stored in portfolios labelled with each participant's reference number and locked in a fire-resistant locker.

2.6 Method overview

Colour discrimination ability was assessed using a battery of colour vision tests. Participants were divided into different age groups, ranging from eight to 66 years. All data were collected by a single operator. The results from the carriers were compared to those of a control group of normal trichromatic females.

2.6.1 Questionnaire

Information concerning the subjects' and their families' colour vision was gathered using a questionnaire (Appendix E) prior to testing. Participants were selected based on the questionnaire's answers. The answers predicted who will be the participants and the total sample. The questionnaire's front page contained subjects' contact information. After testing, the front page was removed and destroyed.

2.6.2 Colour vision tests

The following colour vision tests were used: Ishihara (24 pl. ed.), Hardy-Rand-Rittler fourth edition (HRR 2002), the Neitz Test of colour vision (NTCV), Cambridge Colour Test (CCT), the Farnsworth 100 Hue Test (FM100-Hue), the HMC anomaloscope (both Rayleigh and Moreland match) and the Medmont C-100.

Each test was administrated and performed according to its accompanying guidelines. Test procedures were made for each test and were strictly followed. Subjects under the age of 18 were tested with Ishihara, HRR 2002, the Neitz test of colour vision, FM100-Hue and Medmont C-100. The anomaloscope and CCT-test was only administered to subjects over the age of 18. For Ishihara, HRR 2002, NTCV, FM100-Hue and Medmont C-100, the level of illumination was measured at the surface of the test screen/plates with a digital lux meter (Hagner Model EC1, Hagner AB, Solna, Sweden).

2.6.3 Test conditions

The approximate time required for each test was: Ishihara, 5 min; HRR 2002, 10 min; NTCV, 15 min; CCT, 30 min; FM100-Hue, 15 min; the anomaloscope, 60 min and Medmont C-100, 5 min. This meant that the total expected testing time was approximately 60 minutes for the children, 2.5 hours for the optometry students and 1.5-2.0 hours for all other adults who took part.

The optometry students and the parents of children from Kongsberg were tested in the colour vision laboratory at Buskerud University College, Department of Optometry and Visual Sciences, while the other subjects were tested at primary schools in Kongsberg, Notodden and Bø.

The Medmont C-100 and NTCV tests were performed under a combination of fluorescent lighting and natural daylight in a room with both windows and fluorescent lights.

The Ishihara, HRR 2002 and FM100-Hue tests were performed in a dark room under controlled illumination, whereas the CCT and the anomaloscope tests were performed in a dark room. The windows were covered with curtains and venetian blinds, and these tests were performed inside tents.

2.7 Colour vision tests used

2.7.1 Ishihara 24 plates edition, 2005

The Ishihara (Kanehara trading INC, Tokyo, Japan) is a pseudoisochromatic test and was first published in 1917 (Birch, 1997b, Linksz, 1964b) by the Japanese medical officer Dr. S. Ishihara (Linksz, 1964b). The test measures the subject's discriminative capacity (Ventura et al., 2003) and classifies people as either normal trichromats or colour deficient. It is simple and easy to administer, but provides a probable, rather than certain, diagnosis (Lakowski, 1969b). It is one of the most widely used screening tests for red-green colour deficiency (Birch, 1997b, Dain, 2004a), but does not screen for blue-green deficiencies (Cole et al., 2006, Ishihara, 2005, Dain, 2004a, Birch, 1993). The Ishihara test classifies protan and deutan defects, but it does not grade these deficiencies (Birch, 1993).

The Ishihara test consists of a series of plates, each presenting digits as the figure. There are also some plates for those who cannot read, where some winding paths have to be recognized and traced (Linksz, 1964b, Birch, 1993). Each plate consists of many discrete dots, each dot has its own contour and the luminance of the individual discs is randomized (Birch, 1993). The coloured dots have a chromaticity that lies on or close to protan or deutan confusion lines (Lakowski, 1969b). The dots are positioned in such a way that a figure can achieve different designs (Birch, 1993). The numeral plates are divided into five different categories of design (Linksz, 1964b, Birch, 1997b, Lakowski, 1969b, Dain, 2004a, Birch, 1993). Plate one is an introduction or demonstration plate, containing figures that can be discriminated by both normal and colour deficient people (Birch, 1997b, Linksz, 1964b). Therefore it also serves for malingerers (Linksz, 1964b). Plates two to seven have a transformation design (Birch, 1997b, Ishihara, 2005). Both normal and deficient observers can detect a figure in these plates, but they identify different digits (Lakowski, 1969b,

Linksz, 1964b). It has been claimed that some seemingly colour-normal female carriers sometimes fail these plates (Linksz, 1964b). The design of plates eight to 13 is vanishing (Birch, 1997b, Ishihara, 2005), which means that normal observers read the digits, but colour deficient observers either cannot read them or read them incorrectly (Ishihara, 2005, Lakowski, 1969b). Plates 14 and 15 have a so-called hidden design, which means that the majority of colour deficient observers can identify digits, but normal observers cannot (Linksz, 1964b, Ishihara, 2005). The fifth and last design is the classification design of plates 16 and 17. These plates each contain two digits, which can be identified by normal observers. These plates distinguish protanopes and strong protanomalous observers from deuteranopes and strong deuteranomalous observers (Ishihara, 2005, Linksz, 1964b).

About 40% of normal observers make at least one misreading of the Ishihara test (Birch, 1997b, Neitz and Neitz, 2000) and indeed, colour vision is regarded as normal if 13 or more plates are read correctly. If only nine plates or less are read correctly, then colour vision is regarded as deficient. If three to six mistakes are made, a level of uncertainty is inferred and further examination with an anomaloscope is recommended (Birch, 1997b). Anomalous trichromats are expected not to be able to read some of the plates, while dichromats are expected not to be able to read any (Linksz, 1964b). Children, both with normal and deficient colour vision, make more mistakes than adults (Hill et al., 1982). A study from Sidney, Australia, concluded that 75.8% of children (both sexes, aged 6 years) made one or more confusion errors, 62.7% made one to three errors and 13.1% made more than three errors. These subjects were classified as normal trichromats on other colour vision tests (Cosstick et al., 2005). One in three children who were classified as colour defective aged 5.5 years were found to be normal at age eight, when tested with Ishihara, showing that errors decrease with age. By the age of 11, children have error rates equivalent to those of adults on tests like Ishihara and HRR 2002 (Lloyd et al., 1984).

Ishihara 24 plates edition, 2005: Method

The Ishihara test (Kanehara trading INC, Tokyo) (Ishihara, 2005) was performed binocularly under controlled illumination, in a dark room with the lamp “True Daylight Illuminator with Easel” (colour temperature 6200 K, model number 1339R, Richmond Products, Albuquerque, NM). The plates were held 75 cm from the subject and tilted so that the plane of the paper was at the right angle to the line of vision (Ishihara, 2005). The plates

were illuminated at 1019 (±35) lux in the plane of the plates. The subject was instructed to read the number load and to give their answer within three seconds. Responses were recorded on a scoring sheet (Appendix F).

2.7.2 Richmond Products Hardy-Rand-Rittler 2002

The Richmond Products Hardy-Rand-Rittler 2002 (HRR 2002) fourth edition (Richmond Products, Albuquerque, NM) (Bailey et al., 2004, Cole et al., 2006) is a pseudoisochromatic test for colour vision which includes plates that identify tritan, protan and deutan colour vision deficiencies and grade their severity. It therefore provides the clinician with more information than does the Ishihara (Cole et al., 2006). In the 2002 edition of HRR, the colours on the test plates are moved nearer to the dichromatic confusion lines than in previous editions (Cole et al., 2006, Dain, 2004b), thereby improving the sensitivity of the test (Bailey et al., 2004).

The HRR 2002 consists of 24 plates, each displaying either one or two symbols. The symbols can be a cross, a circle or a triangle and are constructed of coloured dots on a background of grey dots (Birch, 1997a, Cole et al., 2006). The coloured dots have a chromaticity that lies on or close to protan, deutan or tritan confusion lines. There are six screening plates, four for red-green (protan and deutan) colour deficiencies and two for blue-green (tritan).These plates are followed by 14 diagnostic plates, constructed to grade the severity of the deficiency and to differentiate protans, deutans (10 plates) and tritans (four plates) (Cole et al., 2006). In addition to the test plates, there are also four demonstration plates in which the colours of the symbols can be seen by all observers. The demonstration plates are presented at the beginning of the test (Cole et al., 2006, Birch, 1997a).

The test is constructed so that those with a colour vision deficiency will not see the symbols with colours lying on their confusion loci. The deficiency is graded as mild, medium or severe, depending on whether the symbols on the more saturated plates can be seen. If the subject makes two or more errors on the screening plates, he or she will probably have abnormal colour vision (Cole et al., 2006, Birch, 1997a). There is a small risk (1:40) that with this criterion the diagnosis is incorrect and the subject is a normal trichromat. 86% of the time, the HRR 2002 successfully categorizes protans and deutans; 11% of the time subjects remain unclassified and 3% of the time they are incorrectly classified (Cole et al., 2006).

Results obtained with the 2002 edition of HRR are said to correspond closely to those obtained with the anomaloscope (Bailey et al., 2004).

Richmond Products Hardy-Rand-Rittler 2002: Method

The HRR 2002 was performed in the same way as Ishihara, that is, binocularly in a dark room with the "True Daylight Illuminator with Easel" lamp (colour temperature 6200 K, model number 1339R, Richmond Products, Albuquerque, NM). As for the Ishihara, the plates were placed on an angled stand 75 cm from the subject. They were illuminated at 1019 (±35) lux in the plane of the plates. The subject was instructed to identify the symbols and point to them with a pencil within three seconds. Every missed symbol was counted as an error. Responses were recorded on the scoring sheet (Appendix F). If a subject made one or more errors on the screening plates, he or she was tested further with the diagnostic plates.

2.7.3 The Neitz Test of Colour Vision

The Neitz Test of Colour Vision (NTCV) (Western Psychological Services, Los Angeles, CA)(Neitz and Neitz, 2001) is a disposable pencil and paper test developed by Maureen and Jay Neitz, which was first printed in 2001 (Neitz and Neitz, 2001). The test is claimed to detect both main classes of colour deficiency, red-green and blue-yellow and to classify the subtypes of red-green deficiency (protan and deutan) and grade their severity (Neitz et al., 2001). The test consists of one demonstration and eight test panels. Each panel consists of a grey-scale and colour pattern. The colour pattern makes a geometric shape; a set of darker dots suggests an alternative shape that serves as a distraction or as luminance noise in the background. Below each panel there is a multiple choice row, displaying small versions of the possible embedded shapes, which are a circle, a triangle, a square or a diamond (Neitz et al., 2001, Neitz and Neitz, 2001). The plate design is a mixture of the vanishing- and the transformation type. In the vanishing type, the symbols vanish for the colour deficient observer, while in the transformation type, normal and deficient observers identify different figures (Neitz and Neitz, 2001, Neitz et al., 2001). The colours on the dots that make the different shapes fall near the confusion line on the CIE colour diagram when the illumination is natural daylight and fluorescents light (Neitz and Neitz, 2001).

Because there are three versions of the Neitz Test (forms 1, 2 and 3) it is easy to administer and carry out in groups and in classrooms (Neitz et al., 2001). The different forms all contain the same set of stimuli, but present them in a different order. Subjects who make one or more errors on the Neitz Test should be retested with another form of the test. The user manual (2001) claims that it is possible, based on the results of the second test, to establish the probable type and severity of the individual's colour deficiency. The Neitz Test is claimed to be rapid, efficient and reliable for testing colour vision (Neitz and Neitz, 2001).

Neitz Test of Colour Vision: Method

The NTCV was performed binocularly under normal room light conditions, with daylight and fluorescent light. Each subject was handed one of the three versions of the test. When the test instruction was read, pictures of the geometrical shapes were shown to the subject. The subject had to recognize and mark which figure they were able to see on the test sheet. If the subject made one or more errors, he or she was retested with another form of the test. Based on the results of this second testing, the probable type and severity of colour vision deficiency was provided, but this was not a certain diagnosis.

2.7.4 Cambridge Colour Test

The Cambridge Colour Test (CCT) (Cambridge research systems Ltd, Cambridge, UK) is a computerized colour vision test (Ventura et al., 2003), which measures the hue discrimination in a spatial and luminance noise situation (Mollon and Reffin, 1989, Ventura et al., 2003, Regan et al., 1994). The test target is a Landolt C presented on a computer display (Ventura et al., 2003). The target and background are made up of many discrete discs, in a mosaic design. Each disc has its own contour and the luminance of the individual discs is randomized. The target C differs in chromaticity from the background. This type of stimulus array is inspired by principles of traditional pseudoisochromatic tests, such as of the Ishihara and the Stilling (Regan et al., 1994, Mollon and Reffin, 1989, Mollon and Regan, 2000). Because luminance and contour differ on each disc, the subject cannot use such cues to discriminate the target from the background (Regan et al., 1994, Mollon and Regan, 2000).

The C is presented randomly in one of four orientations - up, down, left or right. The subject is instructed to indicate the position of the C opening by pressing the corresponding button on a response box (Ventura et al., 2003, Mollon and Regan, 2000). The difference in chromaticity between the C and the background is adjusted dynamically, according to the subject's performance. A staircase routine (see Figure 2-1) is used to establish the chromaticity difference needed for the subject to reliably report the orientation of the C (Mollon and Regan, 2000) and the subject's threshold discrimination is measured (Ventura et al., 2003). The staircase procedure begins with a saturated hue. Every time the subject makes a correct response, the test proceeds to a less saturated hue. If the response is correct, it is followed by presentation of hues with a lower saturation value and the step size is halved. If the response is incorrect or missing, the following presentation is of a hue with a higher saturation value and the step size is doubled. The series is terminated and the threshold is computed after six incorrect responses or six reversals (Ventura et al., 2003).

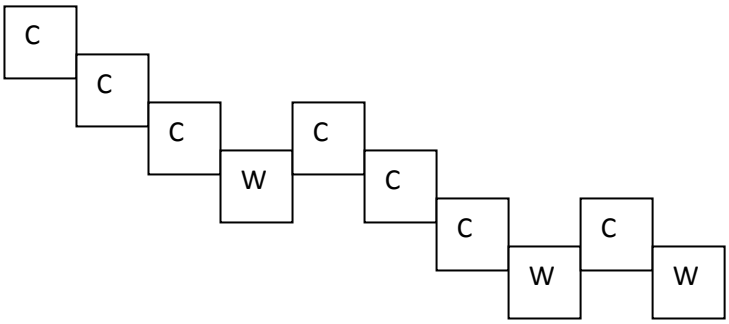

Figure 2-1 CCT's staircase procedure ("C" = correct answer; "W" = wrong answer).

The target differs from the background along one of three theoretically significant lines in colour space in the screening test "Trivector". The three lines are the protan, deutan and tritan confusion lines. The "Ellipse" test is a longer version of the test and yields a full discrimination ellipse (Mollon and Regan, 2000), determined along 20 vector lines (Ventura et al., 2003). The CCT test is in the native space of the Commission Internationale de l'Éclairage (CIE) (1976) u', v' diagram (see 1.11), which is a linear transformation of the CIE (1931) *x, y* chromaticity diagram (Mollon and Regan, 2000, Ventura et al., 2003). The fact that the CCT refers to the colour space of CIE, makes the test an important instrument for testing acquired colour deficiencies as well as small degrees of congenital colour anomaly (Ventura et al., 2003).

Normal subjects are expected to perform below the limits of 100 (protan), 100 (deutan) and 150 (tritan) for their first examination on the CCT Trivector test. On the CCT Ellipse test, normal subjects yield small discrimination ellipses. The axis ratio is expected to be small, typically less than 2.0 (Mollon and Regan, 2000). Subjects with congenital forms of red-green colour deficiency are expected to almost always exceed the normal limits on both the protan and deutan axis of the Trivector test. Protans and deutans are reliably distinguished and it is claimed that results agree with those obtained using the Nagel anomaloscope. The axis of the higher score indicates the type of deficiency. A dichromat is not expected to achieve a round ellipse on the Ellipse test, but rather two parallel lines in the middle of the ellipse (Mollon and Regan, 2000) and they should only see two of the three different stimuli in the Trivector test (Miyahara et al., 2004).

Cambridge Colour Test: Method

The Cambridge Colour Test (CCT) was only administered to the adult subjects. The test was performed binocularly in a dark room, with the subject seated three metre from the screen. LED lights on computers etc. were covered, as these could have distracted subjects during the test. A chin and forehead rest was used, to ensure that the distance between subject and screen was both constant and correct. When seated like this, the gap in the C-ring subtends one degree of visual angle. The subject indicated the orientation of the C by pressing the corresponding button on a response box within three seconds of the onset of the display. The response box automatically beeped when a button was pressed. The subject was instructed to respond only when they saw (or thought they saw) the orientation of the C. They were told to avoiding guessing and not to respond to presentations they did not see. Non-responses and incorrect responses were treated as equivalent. The “Trivector” test was administered first and lasted approximately three to four minutes. It was followed by the “Ellipse” test, which lasted about 20 minutes.

Daily check and calibration

To ensure the stability of the monitor, a daily check of colourimetric measurements was made with a spectrophotometer (SpectraScan ^{PR}650, Photo Research) before any experiments were carried out. The measured area was 1°. The computer display was turned on two hours prior to this daily check. A range of six luminance levels, between two and

16cd/m^2, were used. Along the confusion lines, a maximum excursion of 0.110 units and a minimum excursion of 0.002 units was used. The measured values were recorded. If the values in the displayed CIE (x, y, Y) coordinates exceeded 0.005 in (x, y) and 5% in Y, a calibration (or Gamma correction) was carried out, otherwise the monitor was ready to be used in the experiment.

To perform the calibration, the room illumination was turned off and an OptiCal probe was attached to the monitor. After the calibration, the colour coordinates and luminance (cd/m^2) were checked for the colours Red, Green and Blue. Scale factors were then calculated by taking the ratio of the luminance value measured by the OptiCal and the one measured by the ^{PR}650 for each of the three different colours. The scale factors were incorporated into the tests settings and a new calibration was performed. The specified colours were then measured again to determine whether the calibration had been successful.

2.7.5 The Farnsworth 100 Hue Test

The Farnsworth 100 Hue Test (FM100-Hue) (Munsell color, New Windsor, New York) examines hue discrimination and colour confusion (Kinnear and Sahraie, 2002, Lakowski, 1969b, Farnsworth, 1957) and involves arranging moveable coloured caps in a continuous colour series (Thyagarajan et al., 2007, Kinnear and Sahraie, 2002). The test is based on the recognition of surfaces by reflection (Lakowski, 1969b). Four trays of 85 movable caps cover the entire colour circle (Thyagarajan et al., 2007, Lakowski, 1969b, Farnsworth, 1957); the caps are divided into four groups, one from red to yellow, one from yellow to blue-green, one from blue-green to blue and one from blue to purple-red. The colour difference between the different caps is very small, but the differences for each box are not uniform. The first box, with caps 85 to 21, is the least difficult, the third box, with caps 43 to 63, is the most difficult (Lakowski, 1969b). Consecutive caps are not likely to be discriminated by dichromats: caps 14 to 24 and 57 to 72 for protans, caps 12 to 22 and 52 to 64 for deutans and caps 80 to 9 and 42 to 54 for tritans (Lakowski, 1969b). The mid-point indicates the type of deficiency. Protans have their mid-point between 62 and 70, deutans between 56 and 61 and tritans between 46 and 52 (Farnsworth, 1957). The distribution of errors obtained on the FM100-Hue can be described by the confusion angle (types of colour deficiencies), confusion index (the degree of loss) and or selectivity index (the amount of

polarity or lack of randomness in cap arrangement). Vingrys and King-Smith (1988) have shown that the average protanopic angle is +8.8°, whereas the average deuteranopic angle is -7.4°. To separate normal trichromatic subjects from colour deficient observers, the confusion index should be lower than 1.78 and the selectivity index lower than 2.00 (Vingrys and King-Smith, 1988).

Colour vision changes with age, therefore the normal values for error scores on the FM100-Hue test also change with age. In subjects aged between 20 and 29, the mean FM100-Hue total error score (TES) is at a minimum. It increases for both younger and older groups of subjects (Kinnear and Sahraie, 2002, Smith et al., 1985, Verriest et al., 1982). This means that the performance on FM100-Hue test varies as an U-shape function of age (Kinnear and Sahraie, 2002). It has been suggested that the test is too difficult for children under the age of 10, due to their underdeveloped cognitive skills (Birch, 1997b), which may result in larger error scores that are unrelated to their colour vision abilities (Dain and Ling, 2009). Others, however, have proposed that children understand the concept of seriation, as shown on tests with varying grey levels (Dain and Ling, 2009) and would not, therefore, experience problems in performing the FM10-Hue test. It is not expected to find a difference as a function of sex between colour normal subjects. For observers over the age of 40, or between the ages of 10 and 19 (Smith et al., 1985) blue-yellow sensitivity deteriorates more than red-green sensitivity (Kinnear and Sahraie, 2002). The FM100-Hue is robust to refractive blur - it has been suggested that blur up to +3.0 D does not affect the results of the test (Thyagarajan et al., 2007). 16% of subjects with normal colour vision will have a total error scores that exceeds 100. These subjects have lower colour discrimination than other normal subjects, but they do not exhibit colour defects on tests such as the anomaloscope or on pseudoisochromatic tests (Farnsworth, 1957). It has been assumed that female carriers will have results that fall within the normal error score range on the FM100-Hue test (Jordan and Mollon, 1993b).

The FM100-Hue is said to reliably distinguish between two important axes in colour space, the red-green axis involving changes in L- and M-cone excitation and the tritan axis involving changes in S-cone excitation (Knight et al., 1998). The test detects protan, deutan and tritan deficiencies and colour confusions. It also indicates minute differences in colour discrimination and the results correlate well with similar findings obtained using the

Pickford anomaloscope. The test is therefore claimed to be more accurate than standard pseudoisochromatic tests such as the Ishihara (Lakowski, 1969b).

Farnsworth 100 Hue Test: Method

The Farnsworth 100 Hue Test (FM100-Hue) was performed in a dark room with the True Daylight Illuminator (III 6200 K) lamp. The test was illuminated at 965 (±82) lux in the plane of the caps. The subject was told that the test should take about two minutes per box, but that accuracy was more important than speed. The caps were placed on a non-reflecting white surface in front of the box. Before being presented to the subject, the caps were arranged in random order. The subjects wore white gloves to avoid transferring grease and fingerprints to the coloured caps. The subject was instructed to arrange the moveable caps so that they formed a regular colour series. The total error score was measured and analyzed using an Internet site (http://www.torok.info/colorvision/fm100.htm).

2.7.6 HMC anomaloscope MR Oculus

With the aid of spectral colour mixtures, the HMC anomaloscope MR (Typ 47700, Oculus Optikgeräte GmbH, Germany) is an instrument for testing colour vision, its anomalies and deficiencies (Linksz, 1964a, Oculus, 1999). The earliest editions type of anomaloscope detected and differentiated anomalies and deficiencies in the perception of red and green only (Linksz, 1964a), but newer editions can also detect and classify yellow and blue vision deficiencies (Oculus, 1999, Lakowski, 1969b). The Oculus anomaloscope uses light-emitting diodes as sources (Thomas and Mollon, 2004, Oculus, 1999) and is designed to simulate the classical Nagel anomaloscope (Thomas and Mollon, 2004).

The instrument presents a horizontal, divided, two-part viewing field, where in the Rayleigh match variant the upper field displays a mixed colour field of green and red and the comparison (lower) field presents yellow (Oculus, 1999, Linksz, 1964a, Lakowski, 1969b). In the Moreland match variant, the upper field consists of mixed green and blue, whereas the comparison field consists of cyan and yellow (yellow is used for desaturation of cyan) (Oculus, 1999). In both variants of the test, these two fields have to be matched (Lakowski, 1969b, Linksz, 1964a).

In the Rayleigh match, by mixing a certain spectrum red and a certain spectrum green in specific proportions, it is possible to produce a colour sensation equivalent to that produced by stimulation of the eye with a certain monochromatic spectrum yellow (Linksz, 1964a). This gives the Rayleigh equation (Linksz, 1964a):

$$a\text{Red} + b\text{Green} = c\text{Yellow}$$

The values of the coefficients *a* and *b* can vary from zero to a maximum, but *c*, the sum of *a* and *b*, is constant (Linksz, 1964a). This means that if the amount of green is increased, the same amount of red will be decreased. The Oculus anomaloscope Rayleigh equation is given by (Oculus, 1999):

$$\text{Red (666 nm)} + \text{Green (549 nm)} = \text{Yellow (589 nm)}$$

A normal trichromat will equate the test field with a known proportion of red and green, while for a colour deficient subject the proportion of red and green will vary according to their deficiency type. Compared to subjects with normal trichromatic colour vision, a protanomalous person requires more red light (Ventura et al., 2003), while a deuteranomalous person requires more green (Ventura et al., 2003, Neitz et al., 1996).

The Moreland equation to evaluate normal colour vision is given by (Oculus, 1999):

$$\text{Blue (436 nm)} + \text{Green (490 nm)} = \text{Cyan (480 nm)} + \text{Yellow (589 nm)}$$

The wavelengths of blue and green were selected based on wavelengths confused by tritanopes. Both lens pigment absorbance spectra and subject age are said to affect the matching range and midpoint of the Moreland match (Moreland, 2004). Subjects suffering from diabetes mellitus have a Moreland match midpoint that is shifted towards the blue primary and a widening of the matching range (Kurtenbach et al., 2002). Rods may affect the blue-green colour matching of a colour deficient observer, which may cause a shift in the Moreland match (Pokorny et al., 1981).

Anomaloscope results exhibit seasonal variation, for example, normal trichromatic subjects tend to make matches with a greater proportion of long-wave light during the summer

months. This can be explained by differences in temperature during the different seasons, which affects the instrument's prism (Jordan and Mollon, 1993a).

Three measurements are of interest - the match midpoint, the level of reference yellow and the range of mixtures accepted (Thomas and Mollon, 2004). Some subjects might have a small matching range, accepting only one ratio setting. These are usually normal trichromats. Others may accept a number of ratios and thus have a larger matching range. In this case, a mid-matching point (match midpoint) is usually calculated (Lakowski, 1969b). The level of reference light will betray the nature of the subject's deficiency and will separate the protanope from the deuteranope (Linksz, 1964a, Oculus, 1999).

High chromatic sensitivity is often indicated by a narrow red-green matching range and is typical of normal trichromatic vision. But, the variability of the matching range within normal trichromats is large. This variability makes the direct comparison with colour deficient observers more difficult (Barbur et al., 2008). Some normal trichromats accept many of the red-green mixture ranges, others require significantly more red or green in the match, but accept only a narrow range that is well within the range observed in normal trichromats (Barbur et al., 2008, Lakowski, 1969b). Barbur et al. (2008) found that it is possible to be colour deficient with correspondingly reduced chromatic sensitivity, but at the same time to make normal red-green anomaloscope matches. They suggest that subjects with cone pigment wavelength separations above 20 nm would be classified as normal in conventional colour vision tests and might also produce anomaloscope matches that fall within the normal range. They also claim that there is a poor relationship between the midpoint and the size of the corresponding matching range (Barbur et al., 2008). From a given Rayleigh match, it is usually not possible to predict the photoreceptor properties of an individual observer. This is because different combinations of optical density and peak sensitivity can give the same match (Thomas and Mollon, 2004). Compared to a normal trichromatic subject, a heterozygote carrier is expected to have a larger matching range when tested with the Nagel anomaloscope (Jordan and Mollon, 1993b).

To diagnose red-green deficiencies, the suspected protanope or suspected deuteranope must be able to accept an equation at both ends of the scale, at zero and at 73 (Linksz, 1964a). Scale position 73 is all red to a normal observer, but will appear dark to the protanope. Whatever hue he/she might judge it has, he/she will turn the yellow-control

knob towards a lower value. This will reveal the nature of the deficiency and will distinguish the protanope from the deuteranope (the deuteranope will adjust the yellow-control knob only slightly or not at all) (Linksz, 1964a, Oculus, 1999). Both protanopes and deuteranopes accept the mean normal equation and both threshold equations (Oculus, 1999). Female carriers, of either protan or deutan, do not accept the setting of the normal equation (Linksz, 1964a). An abnormal match is predicted when one half of the field falls on a dichromatic region and the other half falls on a trichromatic region, or when the matching field size is so small that it falls on a dichromatic region (Sharpe et al., 1999). A recent study performed by Baraas et al. (2010) showed that the anomaloscope does not predict performance in more general colour judgments and that the degree of colour constancy was unrelated to both match midpoints and matching ranges. Achromatopsia is characterized by extreme loss of brightness in the direction of red or blue and an increase in brightness in the direction of green (Oculus, 1999).

Although the anomaloscope test is considered to be quite difficult to perform, it is used for the screening of children's colour vision and gives reliable results for children aged 11 and above. It can be used with younger children, but it is not recommended for those under four. It takes longer to establish the matching range with young children, but together with other colour vision tests, it can give reliable results (Lloyd et al., 1984). Young children also tend to prefer a slightly reddish hue to match their standard yellow (Lloyd et al., 1984)

HMC anomaloscope MR Oculus: Method

Both Rayleigh and Moreland matches were determined, for the adult subjects, using the HMC anomaloscope MR (Typ 47700, Oculus Optikergeräte GmbH, Germany). The method used was the one suggested by Linksz (1964a). The test was performed monocularly (with the dominant eye) in a dark room. The subject was instructed to match the upper field with the comparison field below. Subjects used two control knobs. One varied the intensity of the spectrally yellow, lower field and one varied the red-green/blue-green colour mixture of the upper field. The subject looked into the tube, which gave a circular bipartite field size of 2° for the Rayleigh match or 4° for the Moreland match. The subject adjusted the two fields until they looked the same, the match midpoint was then calculated. The red-green/blue-green field was then changed by six units in either direction until the subject reported that the two fields were different. The brightness of the standard yellow field was

then adjusted, in an attempt to obtain a match. The extreme ends of the range (when the subject was no longer able to set a match) were established and the number of scale units between the matching limits was recorded as the match range. The subject reported either same (match) or different (not a match) responses when he/she was comparing the two fields. The Rayleigh match was performed first, followed by the Moreland match. The match midpoint, the level of reference yellow and the range of mixtures accepted (Thomas and Mollon, 2004) were recorded and compared with normal data.

2.7.7 The Medmont C-100 colour vision test

The Medmont C-100 colour vision test (Medmont Pty Ltd, Vermont, Australia) is an LED colour vision screening device (Medmont, w.d., Metha and Vingrys, 1992), which uses flicker photometry to measure relative spectral sensitivity for red and green light (Harris and Cole, 2005a). Two alternating LEDs emit red and green light, respectively, on the test screen (Harris and Cole, 2005a, Medmont, w.d.). The subject adjusts the relative intensity of red/green until he/she achieves minimum or no flicker (Harris and Cole, 2005a). The emitted red and green lights is flickered in rapid alternation with the intensity of one light being variable (Metha and Vingrys, 1992, Harris and Cole, 2005a). The minimum sensation or cessation of flicker appears when the luminance of the two lights are equated, heterochromatic flicker photometry (Metha and Vingrys, 1992).

The test is normally performed binocularly at a distance of 30-50 cm, under normal room light conditions of daylight and fluorescent light (Harris and Cole, 2005a, Medmont, w.d.). In the current study, the test was performed monocularly, with subjects repeating the test four times for each eye. The subject's null-point was the average of the four test results. The null-point lies on a scale between -5.0 to +5.0 and the results are evaluated using the following guidelines (Harris and Cole, 2005a):

Null-point	Description
-5 … -2	Decreased red sensitivity: Protan
-1 … +1	Normal (in rare cases -2 … +2)
+2 … +5	Decreased green sensitivity: Deutan

Table 1 Medmont C-100 null-points and classification

Some normal trichromats may overlap into either the protan or deutan range (-2, +2) (Medmont, w.d.). The device does not always give conclusive results for normal trichromats and can classify them as being borderlines. It is common, therefore, for the test to be administered to subjects who have already failed other colour vision tests, in order to classify their colour deficiency, rather than to detect whether one exists (Metha and Vingrys, 1992). It has been claimed that the Medmont C-100 test categorizes protans and deutans seemingly without error and is therefore the preferred test in a diagnostic setting (Cole et al., 2006, Harris and Cole, 2005a), when the subject has already been diagnosed as red-green colour deficient. The test is also said to give repeatable results (Harris and Cole, 2005a). A previous study (Metha and Vingrys, 1992) has found that colour deficient subjects show less variability and are more precise in their settings than their normal trichromatic peers when tested with the Medmont C-100.

The Medmont C-100 test is also used to identify female carriers of protan deficiencies (Harris and Cole, 2005b, Harris and Cole, 2005a) and it may also identify deutan carriers (Robbins, 2005). Protan carriers will often have reduced luminous sensitivity to red light (Schmidt's sign). Obligatory protan carriers are expected to make protan settings on the Medmont C-100 test (Harris and Cole, 2005b), with an average reading of -1,7 or more negative (Harris and Cole, 2005a). It has also been reported that carrier mothers have mean settings on the same side of zero as their colour deficient sons (Robbins, 2005, Harris and Cole, 2005a). It has also been proposed that deutan carriers have diminished luminous sensitivity to green light, a so-called deutan Schmidt's sign (Robbins, 2005, Harris and Cole, 2005a, Metha and Vingrys, 1992) or de Vries' sign (Jordan and Mollon, 1997) and might be identified by a reading of +2,0 or more on the Medmont C-100 test (Harris and Cole, 2005a).

A similar test, the OSCAR test, is claimed to be reliable in distinguishing deutans from protans, but is not ideal for screening colour deficiencies. To distinguish between dichromats and abnormal trichromats, the anomaloscope must be used (Jordan and Mollon, 1997).

Medmont C-100 colour vision test: Method

Every subject was first tested with the Medmont C-100 colour vision test (Metha and Vingrys, 1992). The test was performed monocularly; the dominant eye was tested first. The subject held the Medmont C-100 in both hands, at a distance of approximately 30 to 50cm, with the stimulus test screen facing them, whilst operating the knob with their right hand. The subject adjusted the relative intensities until they achieved minimum or no flicker. Once the point of minimum flicker was detected, the subject was asked to rock the knob backwards and forwards a small amount, so that they could be sure that it was indeed the range with minimum or no flicker. The procedure was repeated four times on each eye. The average of these results was recorded as the subject's null-point (Medmont, w.d.). The test was performed under normal room light conditions, with daylight and fluorescent light. Subjects wore their distance power if needed and those who were presbyopic or needed correction for close work, wore their reading glasses.

The average dominant wavelengths are 569 and 626, respectively, for green and red and stimulus luminance is approximately 2.2cd/m^2. At a working distance of 300 mm, the stimulus field is 1 degree (Medmont, w.d.).

3 Results

3.1 Questionnaire

At the end of the recruitment period, a total of 100 normal trichromatic females and 30 obligate female carriers were enrolled in the study. Of the carriers, eight were carriers of a protan deficiency and 22 were carriers of a deutan deficiency. All the carriers in this study were known, obligate carriers, where the status as a carrier was inferred from the status of the colour vision of her son/father, measured either by the questionnaire or by colour vision testing.

The age of the normal trichromatic females ranged from nine to 38 years, with a median age of 19.5 years and an average age of 18.28 (±7.11) years (one standard deviation in parenthesis). The age of the protan carriers ranged from nine to 41 years, with a median age of 37.5 years and an average age of 31.13 (±13.43) years. The age of the deutan carriers ranged from nine to 66 years, with a median age of 37.5 years and an average age of 32.41 (±16.46) years. Results are presented for four different age groups: 9-12, 18-29, 30-39 years and over 40 years. The carriers in the three youngest age groups were age-matched with normal trichromatic females. Disregarding the female carriers aged over 40, the age of the remaining obligate female carriers ranged from nine to 39 years, with a median age of 22.5 years and an average age of 24.55 (±12.58) years. The age distribution for both the normal trichromatic females and the protan and deutan carriers is presented in Table 2.

Age group	Normal trichromatic female		Protan carriers		Deutan carriers	
9-12	39	(10,79 ± 1,03)	2	(9,50 ± 0,71)	5	(10,34 ± 1,34)
18-29	53	(21,51 ± 2,61)	-	-	4	(21,25 ± 2,50)
30-39	8	(33,38 ± 2,50)	5	(37,80 ± 1,30)	4	(36,50 ± 3,11)
40+	-	-	1	(41,00 ± 0,00)	9	(47,78 ± 8,10)
Sum	100	(18,28 ± 7,11)	8	(31,13 ± 13,43)	22	(32,41 ± 16,46)

Table 2 Age distribution of the female participants. Number of participants with mean age and 1 SD in parenthesis, presented for normal trichromatic females, protan and deutan carriers for four different age groups.

The normal trichromatic females had a spherical-cylindrical equivalence of OD: -0.76 (±2.43) DS and OS: -0.73 (±2.40) DS (one standard deviation in parenthesis). The female carriers had a spherical-cylindrical equivalence of OD: -0.17 (±1.32) DS and OS: -0.11 (±1.31) DS.

Seventy-five of the 100 normal trichromatic females and 14 of the 30 female carriers had previously had their colour vision tested. Almost an equal proportion of the normal trichromatic females (3.0%) and the carriers (3.3%) complained about problems differentiating and discriminating different colours. The normal trichromatic females reported problems in differentiating dark blue and black, dark violet and grey and dark blue and dark green. The carriers reported problems in distinguishing light pink from light red. Neither the normal females nor the female carriers had any systemic diseases or were taking any medicine that might affect their colour vision. All the female carriers were of Caucasian origin, whilst two of the normal trichromatic females were of Asian origin and three were of African origin.

None of the normal trichromatic females knew about colour deficient relatives. Sixteen of the female carriers knew that their father was colour deficient, three knew that their son was colour deficient, four knew that both their father and their son(s) were colour deficient and seven knew that either their father or their son plus another relative were colour deficient.

3.2 Pseudoisochromatic tests

3.2.1 Carriers' and normal trichromats' performance on PIC-plate tests

Results are presented for the four different age groups in Figure 3-1, Table 3 and Table 4.

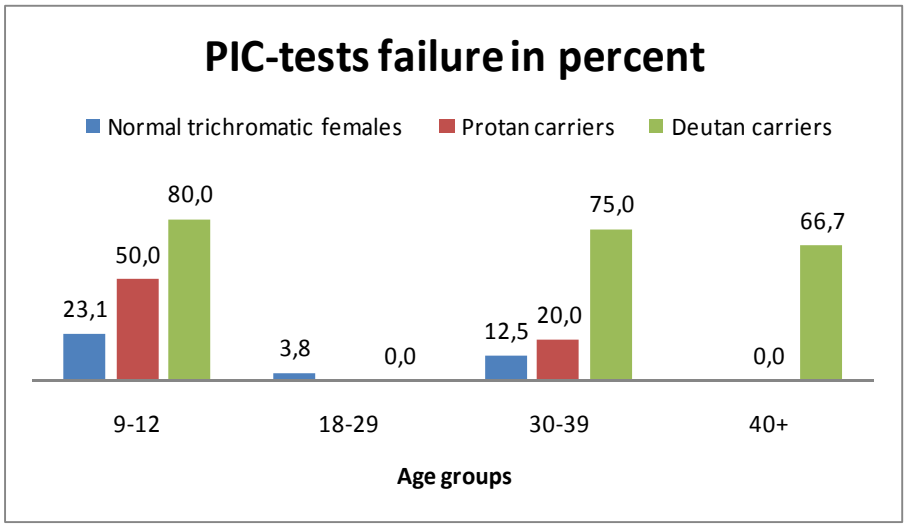

Figure 3-1 PIC-tests failure in percent (subjects who failed one or more PIC-tests), presented for normal trichromatic females, protan carriers and deutan carriers for four different age groups.

PIC TEST		No.	Ishihara	HRR	NTCV	Ishihara & NTCV	All 3 PIC tests
Normal trichromatic females	9-12	39	15,4	5,1	10,3	2,6	2,6
	18-29	53	1,9	-	1,9	-	-
	30-39	8	-	-	12,5	-	-
	Total	*100*	*7,0*	*2,0*	*6,0*	*1,0*	*1,0*
Protan carriers	9-12	2	50,0	-	-	-	-
	18-29	0	-	-	-	-	-
	30-39	5	-	20,0	-	-	-
	40+	1	-	-	-	-	-
	Total	*8*	*12,5*	*12,5*	-	-	-
Deutan carriers	9-12	5	40,0	40,0	40,0	-	20,0
	18-29	4	-	-	-	-	-
	30-39	4	50,0	-	50,0	25,0	-
	40+	9	11,1	22,2	33,3	-	-
	Total	*22*	*22,7*	*18,2*	*31,8*	*4,5*	*4,5*

Table 3 Total percentage of subjects who failed either of the different PIC-tests presented for normal trichromatic females, protan and deutan carriers for the PIC-tests Ishihara, HRR 2002 and NTCV (Failing criteria: Ishihara: three or more misreadings, HRR: Two or more misreadings, NTCV: One or more misreading). The two last columns show percentage of subjects who either failed two of the tests (Ishihara and NTCV) or all three PIC-tests (the three previous columns also include these subjects).

Figure 3-1 shows the percent of normal trichromatic females, protan carriers and deutan carriers who failed one or more of the PIC-tests. Carriers aged 9-12 years failed the PIC-

tests more often than their normal trichromatic peers; 50% of protan carriers and 80% of deutan carriers failed, compared to approximately 20% of their peers. In this age group, 50% of protan carriers and 60% of deutan carriers failed one of the PIC-tests, whereas about 20% of deutan carriers failed all three tests (Table 3). Conversely, all protan carriers in this age group failed only one PIC-test. About 18% of the normal trichromatic females failed one of the PIC-tests and about 5% failed two or three.

None of the carriers aged 18-29 years failed any PIC-tests, whereas almost 4% of their normal trichromatic peers failed one test.

Carriers aged 30-39 years failed PIC-tests more often than their normal trichromatic peers (Figure 3-1). Almost 20% of the protan carriers in this age group failed one or more PIC-tests, compared to approximately 12% of their normal trichromatic peers. 75% of the deutan carriers in this age group failed one or more PIC-tests.

The obligatory carriers aged 40 years and older were not age-matched with normal trichromatic peers; hence comparison with controls was not possible. In this oldest age group, none of the protan carriers failed any of the PIC-tests. Fewer deutan carriers in this age group failed PIC-tests compared to the deutan carriers in both the 9-12 and 30-39 age groups (Figure 3-1).

When age was disregarded, about 59% of the deutan carriers, 25% of the protan carriers and 12% of the normal trichromatic females failed one or more PIC-tests.

	Misreadings Ishihara	No.	0	1	2	3	>3
Normal trichromatic females	9-12	39	46,2	30,8	7,7	10,3	5,1
	18-29	53	66,0	26,4	5,7	1,9	-
	30-39	8	75,0	25,0	-	-	-
	Total	*100*	*59,0*	*28,0*	*6,0*	*5,0*	*2,0*
Protan carriers	9-12	2	50,0	-	-	50,0	-
	18-29	0	-	-	-	-	-
	30-39	5	60,0	20,0	20,0	-	-
	40+	1	100,0	-	-	-	-
	Total	*8*	*62,5*	*12,5*	*12,5*	*12,5*	-
Deutan carriers	9-12	5	-	40,0	20,0	20,0	20,0
	18-29	4	75,0	25,0	-	-	-
	30-39	4	25,0	25,0	-	50,0	-
	40+	9	33,3	22,2	33,3	-	11,1
	Total	*22*	*31,8*	*27,3*	*18,2*	*13,6*	*9,1*

Table 4 The total percentage of numbers of misreadings made on Ishihara. The results are presented for normal trichromatic females, protan carriers and deutan carriers for four different age groups.

Ishihara

Table 3 shows the percent of subjects who failed the different PIC-tests, and Table 3Table 4 shows how many misreadings the different age groups made on Ishihara (the results are presented for normal trichromatic females, protan carriers and deutan carriers). 7% of the normal trichromatic females failed the Ishihara test (that is, made three or more misreadings), while 12.5% of protan carriers and 22.75% of deutan carriers failed the test. The normal trichromatic females who failed the Ishihara test made between three and five misreadings, while the obligate carriers made between three and eight misreadings. 2% of the normal trichromatic females and 9% of the deutan carriers made more than three errors, whereas none of the protan carriers made more than three errors.

HRR

All the subjects who misread one or more plates on the HRR 2002 test misread plate seven. 24% of the normal trichromatic females, approximately 38% of the protan carriers and approximately 41% of the deutan carriers failed plate seven. The failure rate was lower

when subjects were re-tested, when percentages were 2.0, 12.5 and 18.2, respectively (Table 3).

NTCV

None of the protan carriers failed the NTCV test, while 32% of the deutan carriers failed the test (that is, made one or more misreading) (Table 3). Of the deutan carriers who failed the test, 86% failed test panel nine (the most desaturated panel for deutan deficiencies). Approximately 43% of the deutan carriers, whom failed the test, failed two plates (one plate in addition to plate nine: plate four (protan behaviour 3), plate seven (deutan behaviour 2) or plate eight (deutan behaviour 1)). 6% of the normal trichromatic females failed NTCV. All of the subjects who had failed more than one PIC-test also failed NTCV.

3.2.2 Cambridge Colour Test

Nine obligatory carriers and 61 normal trichromatic females were tested with the CCT test. The age of the obligate carriers ranged from 20 to 66 years, with a median age of 32.0 years and an average age of 33.56 (±14.98) years. The age of the normal trichromatic females ranged from 18 to 38 years, with a median age of 21.0 years and an average age of 23.07 (±4.79) years. Because only one protan carrier was tested with CCT, the protan and deutan carriers were analyzed as one group. The results are presented in Figure 3-2. One standard deviation is presented in parenthesis after mean values.

Trivector test

Compared to the normal trichromatic females, the obligatory carriers exhibited higher error scores on all three axes. There was a statistically significant difference between the two groups' scores along the protan and deutan axis (ANOVA: f = 8.49 and 6.81, d.f. = 1, $p < 0.05$), with the carriers producing higher scores on both protan and deutan axes. The carriers and the normal trichromatic females exhibited 93.67 (±62.41) and 64.46 (±19.33), respectively, along the protan axis and 85.33 (±30.41) and 64.95 (±20.47), respectively, along the deutan axis (one standard deviation in parenthesis). There was no statistically significant difference between the two groups' scores along the tritan axis (ANOVA: f = 0.81, d.f. = 1, $p = 0.37$). The carriers and their peers exhibited 98.89 (±34.09) and

90.16 (±26.14), respectively, along the tritan axis. The data are presented in Figure 3-2. Neither the normal trichromatic females nor the obligatory carriers exceeded, on average, the expected upper limits of the CCT trivector test.

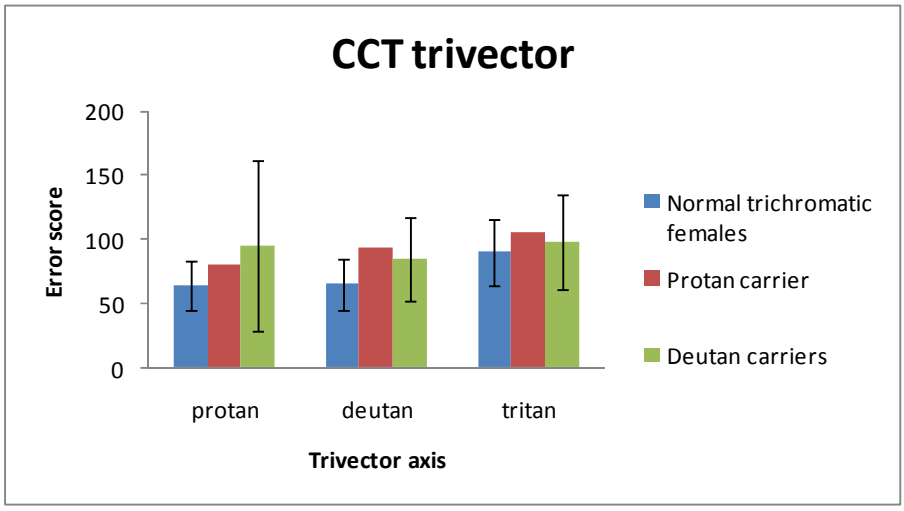

Figure 3-2 CCT trivector scores presented for obligate carriers and their normal trichromatic peers. The columns represents mean error scores and the error bars 1SD. Here the obligate carriers are divided into deutan and protan carriers. Subjects with normal trichromatic colour vision are expected to perform below the limits 100 (protan), 100 (deutan) and 150 (tritan).

Ellipse test

There was no significant difference between the scores from the two groups, either for length or angle on the CCT ellipse test (ANOVA: f = 1.68 and 0.77, d.f. = 1, p = 0.2 and 0.38, respectively). The carriers and their normal trichromatic peers exhibited 81.18 (±47.81) and 67.11 (±27.29), respectively, for angle and 0.02 (±0.005) and 0.018 (±0.005), respectively, for length. The difference between the two groups in the axis ratio was significant (ANOVA: f = 4.34, d.f. = 1, $p < 0.05$). The obligate carriers and their normal trichromatic peers exhibited 1.21 (±0.06) and 1.36 (±0.21), respectively, on the axis ratio.

3.3 Colour discrimination ability

Colour discrimination ability was evaluated and assessed by the Farnsworth Munsell 100 Hue test (FM100-Hue). All the normal trichromatic females and carriers were tested. The results are presented for the four different age groups in Table 5, Table 6, Table 7, Figure 3-3 and Figure 3-4

3.3.1 Protan and deutan carriers

Of the 30 obligate carriers tested with FM100-Hue, eight were carriers of protan deficiencies, and 22 were carriers of deutan deficiencies. There was no significant difference in the square root of total error score (TES) between the normal trichromats, protan carriers and deutan carriers in any of the age groups (ANOVA: 9-12: f = 0.59, d.f. = 2, p = 0.56, 18-29: f = 1.78, d.f. = 1, p = 0.19, 30-39: f = 3.07, d.f. = 2, p = 0.08, 40+: f = 1.48, d.f. = 1, p = 0.26).

When age was disregarded, there was still no significant difference in the square root of total error score (TES) between the protan and deutan carriers (ANOVA: f = 0.72, d.f. = 1, p = 0.4), nor was there any difference between the normal trichromats, the protan carriers and the deutan carriers (ANOVA: f = 0.63, d.f. = 2, p = 0.53).

FM100-Hue & PIC-tests		No.	FM100-Hue	Both FM100-Hue & PIC-tests
Normal trichromatic females	9-12	39	23,1	7,7
	18-29	53	35,9	1,9
	30-39	8	25,0	-
	Total	*100*	*30,0*	*4,0*
Protan carriers	9-12	2	-	-
	18-29	0	-	-
	30-39	5	60,0	20,0
	40+	1	-	-
	Total	*8*	*37,5*	*12,5*
Deutan carriers	9-12	5	40,0	20,0
	18-29	4	50,0	-
	30-39	4	75,0	75,0
	40+	9	33,3	33,3
	Total	*22*	*45,5*	*31,8*

Table 5 FM100-Hue and PIC-tests: The table shows total percentage who failed FM100-Hue (exceeded age matched TES limit) and the percentage who failed both FM100-Hue and one or more PIC-tests. The data are presented for four age groups for normal trichromatic females, protan carriers and deutan carriers.

Table 5 shows the percentage of subjects who failed the FM100-Hue alone and both FM100-Hue and one or more PIC-tests. A higher percentage of the deutan carriers failed

the FM100-Hue test (exceeded the expected upper limit error score for given age (according to Kinnear and Sahraie, 2002)) when compared to both protan carriers and normal trichromatic females. This is evident in all four age groups. Several more deutan carriers failed both FM100-Hue test and one or more PIC-tests, compared to both protan carriers and the normal trichromatic females.

The distribution of errors obtained on the FM100-Hue were never specific for the type of the deficiency the carriers possessed, and there was no significant difference in confusion angle (types of colour deficiencies) (ANOVA: f = 0.49, d.f. = 1, p = 0.49), confusion index (the degree of loss) (ANOVA: f = 61, d.f. = 1, p = 0.442) or selectivity index (the amount of polarity or lack of randomness in cap arrangement) (ANOVA: f = 0.02, d.f. = 1, p = 0.97) between deutan and protan carriers. The selectivity and confusion index are presented in Table 6.

FM100-Hue		Protan carriers	Deutan carriers
Selectivity index	Mean	1,34	1,34
	1 SD	0,20	0,16
	Range min	1,06	1,07
	Range max	1,64	1,69
	No. > 2,0	None	None
Confusion index	Mean	1,73	1,90
	1 SD	0,37	0,59
	Range min	1,24	1,20
	Range max	2,16	3,50
	No. > 1,78	50 %	50 %

Table 6 FM100-Hue: The table show selectivity index and confusion index for protan and deutan carriers. The table also shows how many percent of protan and deutan carriers who exceeded the normal limits of selectivity index and confusion index.

3.3.2 Normal trichromatic females vs. obligate carriers

Since there was no significant difference in the square root TES between normal trichromats, protan carriers and deutan carriers in any of the age groups, the protan and deutan carriers are further analyzed and presented as one group, obligate carriers, in the remaining description of the results for FM100-Hue test.

The youngest age group exhibited, on average, the highest error score. Furthermore, both the obligatory carriers and their normal trichromatic peers in this age group made, on average, more errors on the FM100-Hue than the older age groups (see Table 7 and Figure 3-3). This difference was still significant after a Bonferroni correction had been applied (ANOVA: f = 24.58, d.f. = 3, $p < 0.001$). However, following Bonferroni correction, there was no significant difference in the error scores between the three oldest age groups.

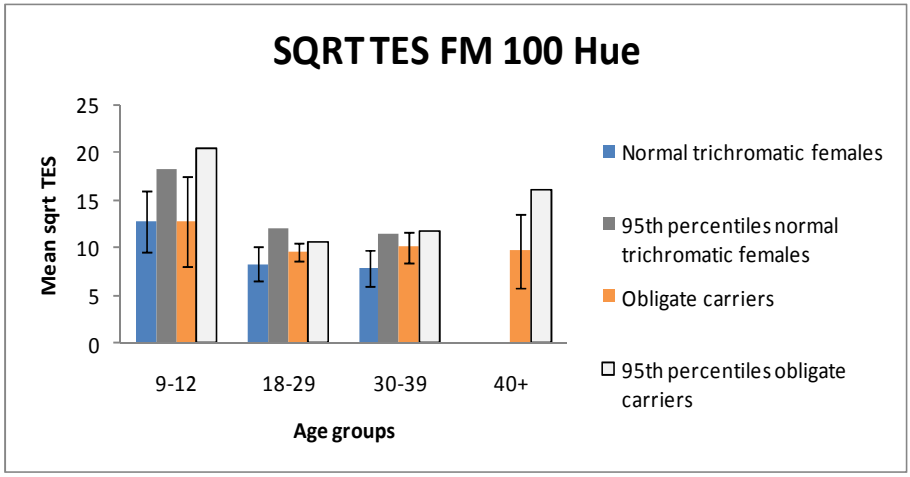

Figure 3-3 SQRT TES FM100-Hue. Mean square root of TES and 95th percentiles are presented for normal trichromatic females and obligate carriers. The error bars represent one standard deviation.

There was no significant difference in the square root error scores (TES) between the obligatory carriers and their normal trichromatic peers in either the 9-12 age group (ANOVA: f = 0.59, d.f. = 2, $p = 0.56$), or the 18-29 and 30-39 age groups (ANOVA: f = 1.78, d.f. = 1, $p = 0.19$) (Figure 3-3 and Table 7).

There was no significant difference in the square root TES between the over 40 age group and the three younger age groups of carriers (ANOVA: f = 1.43, d.f. =3, $p = 0.26$) (Figure 3-3 and Table 7).

For the obligatory carriers, the difference in the variability (square of one standard deviation) in the FM100-Hue error scores was significantly greater (Student-t: t = 3.62, d.f. = 43, $p < 0.001$) for the 9-12 age group compared both to their normal trichromatic peers in the same age group and to carriers and normal trichromatic females in the older groups (Table 7, third row).

TES (SQRT TES)	Normal trichromatic females			Obligatory carriers			
	9-12	18-29	30-39	9-12	18-29	30-39	40+
Mean TES	173,74 (12,80)	71,94 (8,29)	65,50 (7,91)	183,29 (12,80)	91,00 (9,51)	103,44 (10,06)	107,70 (9,69)
1 SD	82,63 (3,18)	31,82 (1,79)	31,85 (1,85)	134,9 (4,77)	17,38 (0,91)	31,53 (1,61)	86,37 (3,91)
Variance	6828,20 (10,10)	1012,21 (3,21)	1014,57 (3,41)	18198,91 (22,75)	302,00 (0,83)	994,28 (2,59)	7458,90 (15,32)

Table 7 FM100-Hue TES for both normal trichromatic females and obligatory carriers (square root of TES is in parenthesis).

These results imply that colour discrimination as assessed by the FM100-Hue test improves with age for both the normal trichromatic females and the obligatory carriers (Figure 3-3 and Figure 3-4). However, the carriers' performance was, on average, poorer than that of the normal trichromats. A total of 30% of the normal trichromatic females and 43.33% of the obligate carriers exceeded the age-matched upper limit of TES. For normal trichromatic females and carriers aged 18 years and older, approximately 15% and 39%, respectively, exceeded a total error score of 100.

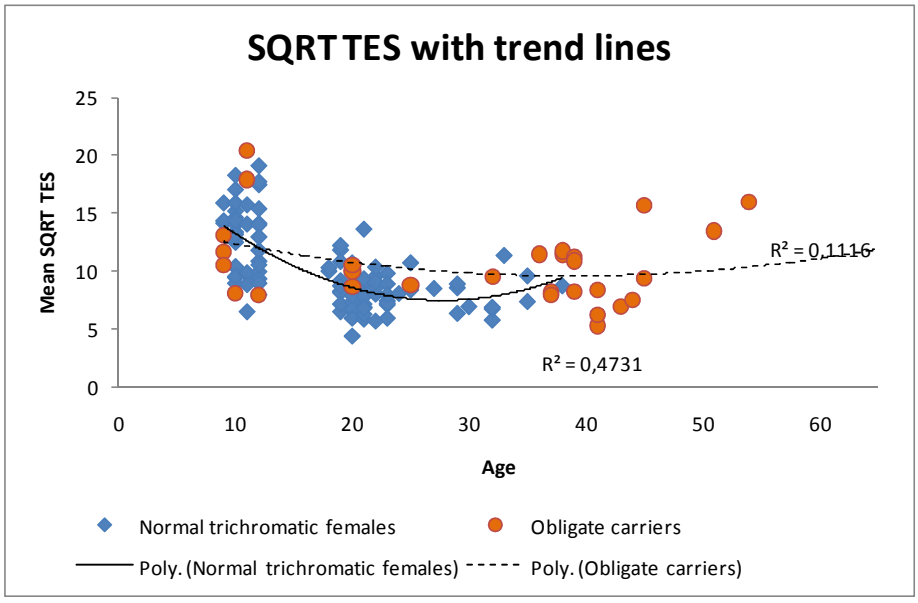

Figure 3-4 SQRT TES FM100-Hue: Distribution of all normal trichromats' and obligate carriers' square root of TES values, presented with second order polynomial trend lines

3.4 Anomaloscopy

3.4.1 Rayleigh match

All participants aged 18 years or older were tested on the Rayleigh match (Oculus anomaloscope). A total of 22 obligatory carriers, aged 18-54, were tested. Six were carriers of protan deficiencies and 16 were carriers of deutan deficiencies. Sixty-one normal trichromatic females, aged 18-38, were tested. The results are presented in Figure 3-5, Figure 3-6 and Figure 3-7. One standard deviation is presented in parenthesis after mean values.

Normal values of matching range and matching midpoint for the instrument used in this study were established from the results of the 61 normal trichromatic females, using the method outlined earlier (see 2.7.6). The distribution of the normal trichromatic females' matching midpoints (rounded numbers) are presented in Figure 3-5. The Rayleigh match midpoint's 95% percentiles ranged from 36.37 to 45.00 for the normal trichromatic females. The midpoints were assumed to follow a normal distribution, with a skewness of 0.136 and a Kurtosis value of 0.202.

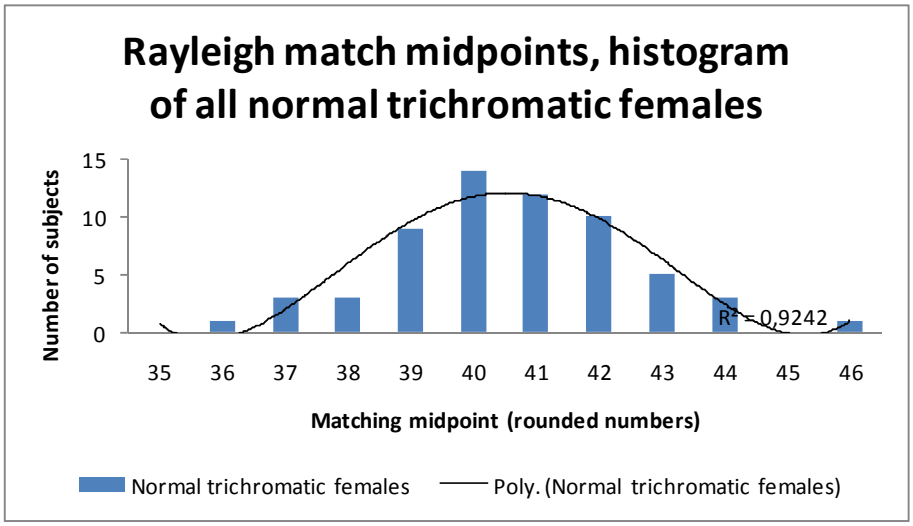

Figure 3-5 Rayleigh match: Distribution of normal trichromatic females' match midpoints (rounded numbers), displayed with a fourth order polynomial trend line.

Figure 3-6 shows the matching range, matching midpoints and matching luminance for normal trichromatic females, protan carriers and deutan carriers. After a Bonferroni correction, there was a significant difference in Rayleigh match midpoints between deutan

and protan carriers and between deutan carriers and their normal trichromatic peers (ANOVA: f = 6.07, d.f. = 2, $p < 0.01$). However, there was no significant difference in Rayleigh match midpoints between protan carriers and their normal trichromatic peers. The normal trichromatic females had a mean matching midpoint of 40.54 (±1.94) on the Rayleigh match. Deutan carriers required, on average, more green, with a mean matching midpoint of 38.74 (±2.35). The mean matching midpoint was also shifted for the protan carriers, who required, on average, more red on the Rayleigh match, with a mean matching midpoint of 41.38 (±1.72).

Compared to the normal trichromatic females, both protan and deutan carriers had a larger matching range of 1.97 (±1.06), 2.90 (±1.08) and 2.08 (±1.33), respectively. This difference was not, however, significant between any of the three groups (ANOVA: f = 1.88, d.f. = 2, $p = 0.531$). The results are presented in Figure 3-6.

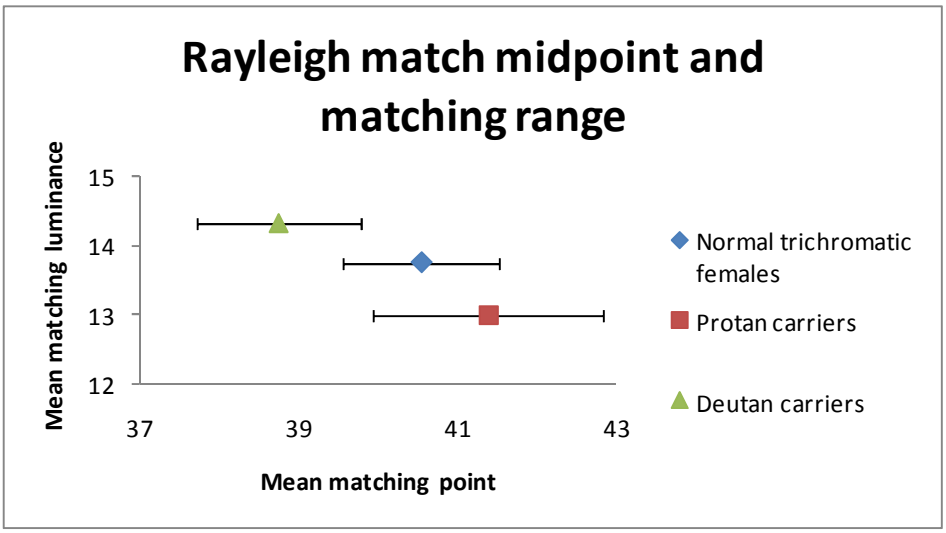

Figure 3-6 Rayleigh match mean midpoint and mean matching luminance presented for normal trichromatic females, protan carriers and deutan carriers. The error bars represent mean matching range.

Protan carriers also set matching luminance below that of normal trichromats and deutan carriers (see Figure 3-6). The difference in average matching luminance between protan and deutan carriers was significant (ANOVA: f = 3.71, d.f. = 2, $p < 0.05$), with an average matching luminance of 12.99 (±0.94) and 14.32 (±1.01), respectively. There was no significant difference in average matching luminance between protan carriers and their normal trichromatic peers or between deutan carriers and their normal trichromatic peers

(ANOVA: f = 3.71, d.f. = 2, p = 0.22 and 0.14). Normal trichromatic females set mean matching luminance, on average, to 13.75 (±1.09).

When the subjects who were classified as having abnormal colour vision by the FM100-Hue were compared to the subjects classified with poor colour discrimination by the same test, those with abnormal colour vision on FM100-Hue did not have a significantly larger matching range on the Rayleigh anomaloscopy (ANOVA: f = 1.54, d.f. = 62, p = 0.14). This applied to both the normal trichromatic females and to the obligate carriers. The results are presented in Figure 3-7.

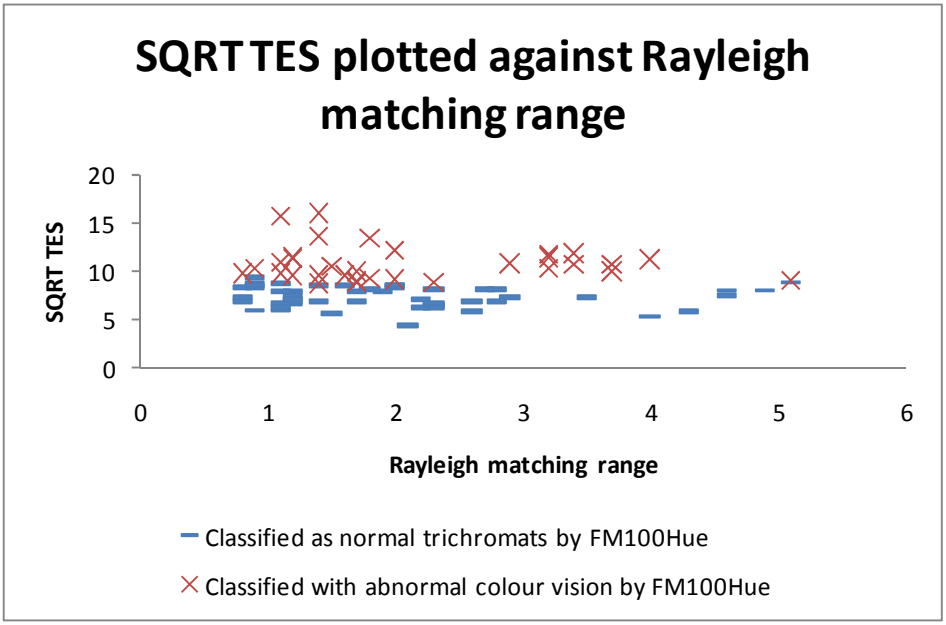

Figure 3-7 Rayleigh matching range plotted against SQRT TES, presented for subjects classified as normal trichromats and subjects classified with poor colour discrimination by the FM 100Hue (regardless of whether they are carriers or not).

3.4.2 Moreland match

All participants aged 18 years or older were tested on the Moreland match (Oculus anomaloscope). A total of 20 obligatory carriers, aged 20-54, were tested. Six were carriers of protan deficiencies and 14 were carriers of deutan deficiencies. Sixty-one normal trichromatic females, aged 18-38, were tested. The results are presented in Figure 3-8, Figure 3-9 and Figure 3-10. One standard deviation is presented in parenthesis after mean values.

Normal values of matching range and matching midpoint for the instrument used in this study were established from the results of the 61 normal trichromatic females, using the method outlined earlier (see 2.7.6). The Moreland match midpoint's 95% percentiles ranged from 44.96 to 60.89 for the normal trichromatic females. The midpoints were assumed to follow a normal distribution, with a skewness of 0.031 and a Kurtosis value of -0.461. The distribution of normal trichromatic females' matching midpoints (rounded numbers) are presented in Figure 3-8.

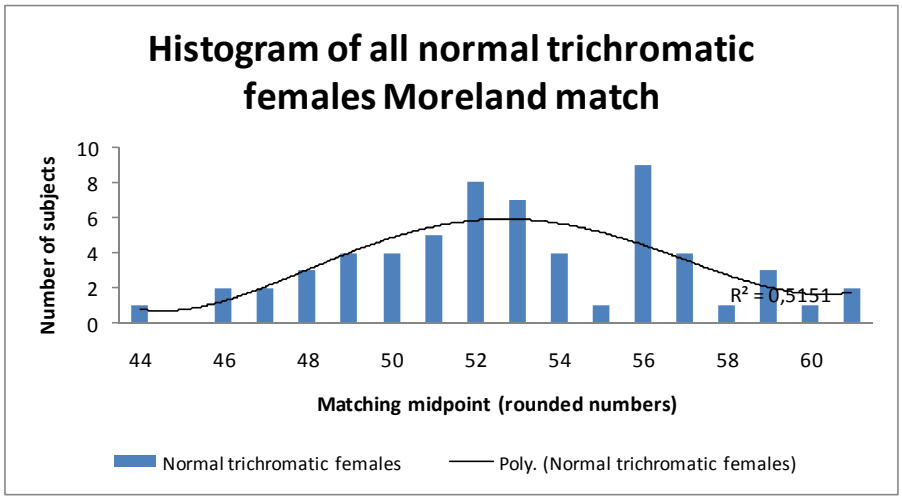

Figure 3-8 Distribution of normal trichromatic females' match midpoints (rounded numbers) on Moreland match, displayed with a fourth order polynomial trend line.

There was no significant difference in the Moreland match midpoints (ANOVA: f = 2.90, d.f. = 2, *p* = 0.061), matching ranges (ANOVA: f = 2.09, d.f. = 2, *p* = 0.13) and matching luminance (ANOVA: f = 1.73, d.f. = 2, *p* = 0.18) between protan carriers, deutan carriers and their normal trichromatic peers. The normal trichromatic females had a mean matching midpoint of 52.90 (±3.87) on the Rayleigh match, values for the protan and deutan carriers were 50.72 (±3.25) and 49.70 (±7.89), respectively. Deutan carriers had a larger matching range compared with both their normal trichromatic peers and protan carriers, with matching ranges of 8.76 (±9.72), 4.74 (±6.10) and 4.60 (±3.77), respectively. The data are presented in Figure 3-9 and Figure 3-10.

Both protan and deutan carriers set matching luminance below that of the normal trichromats, but this difference was not significant (ANOVA: f = 1.73, d.f. = 2, *p* = 0.18). The protan carriers set their matching luminance to 43.28 (±2.06), the deutan carriers to

43.91 (±6.91) and the normal trichromatic females to 45.71 (±3.51). The data are presented in Figure 3-9 and Figure 3-10.

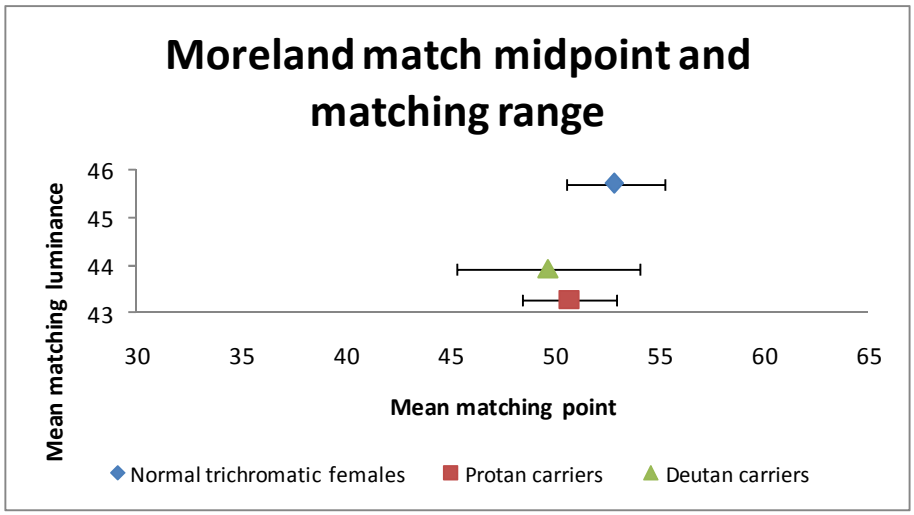

Figure 3-9 Moreland match mean midpoint and mean matching luminance, presented for normal trichromatic females, protan carriers and deutan carriers. The error bars represent mean matching range.

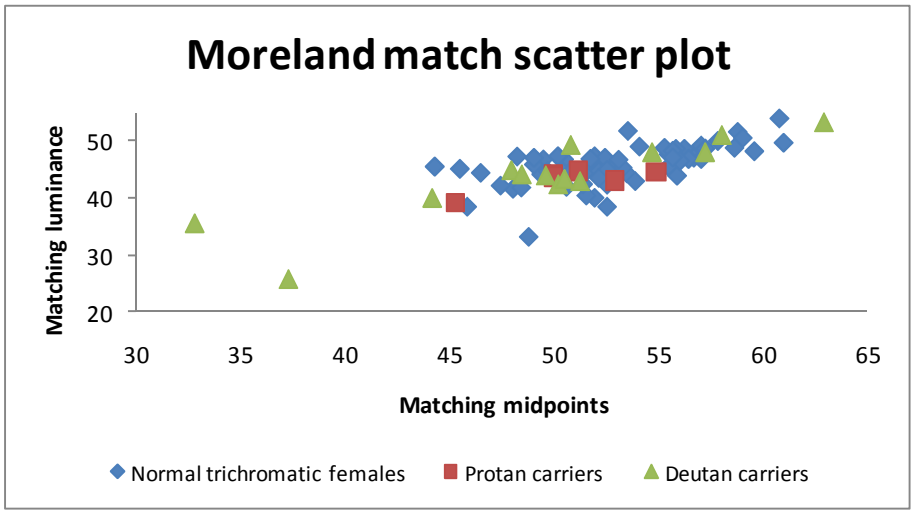

Figure 3-10 Distribution of match midpoints and matching luminance on Moreland match, presented for normal trichromatic females, protan carriers and deutan carriers.

3.5 The Medmont C-100 colour vision test

All participants were tested on the Medmont C-100. A total of 30 obligatory carriers, aged nine to 66, were tested. Eight were carriers of protan deficiencies, and 22 were carriers of deutan deficiencies. Ninety-nine normal trichromatic females, aged nine to 38, were tested.

The results are presented in Figure 3-11, Figure 3-12, Figure 3-13 and Figure 3-14. Error of mean is presented in parenthesis after mean values.

The normal trichromatic females' null-points were assumed to be normally distributed, with a skewness of 0.08 and a Kurtosis value of 1.58 (Figure 3-11). Almost 80% of the normal trichromatic females set their null-points within plus/minus one standard deviation and 94% set their null-points within two standard deviations. 15% of the normal trichromatic females set their null-points between -1 and +1.

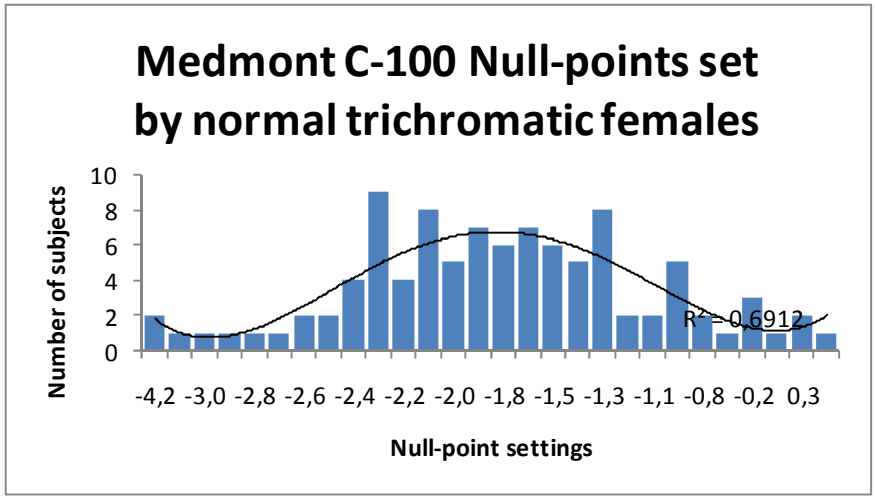

Figure 3-11 Medmont C-100: null-points of 99 normal trichromatic females, displayed with a fourth order polynomial trend line.

When age is disregarded, the Medmont C-100 failed to identify protan and deutan carriers. The null-points of all three groups tested overlapped considerably. Protan carriers used, on average, more red in their colour mixtures than both deutan carriers and their normal trichromatic peers. Deutan carriers used, on average, slightly more green in their colour mixtures. These differences were not, however, significant, either for protan carriers compared to their normal trichromatic peers (Student-t: t =1.16, d.f. = 105, p = 0.12), deutan carriers compared to their normal trichromatic peers (Student-t: t =0.62, d.f. = 119, p = 0.27) or protan carriers compared to deutan carriers (Student-t: t = 1.67, d.f. = 28, p = 0.053). Hence, it was not possible to differentiate either protan or deutan carriers from their normal trichromatic peers. The protan carriers set their null-point to -2.67 (±0.90), the deutan carriers to -1.22 (±0.85) and the normal trichromatic females to -1.73 (±0.81). There were no significant differences between the measurements taken from the right and left

eyes (One-Way repeated measures ANOVA: f = 1.15, d.f. = 7, p = 0.34). For the Medmont C-100 test, only the standard error of mean is presented. This is because the average of eight individual measures constitutes the subject's null-point. The null-points and standard errors of mean are presented in Figure 3-12.

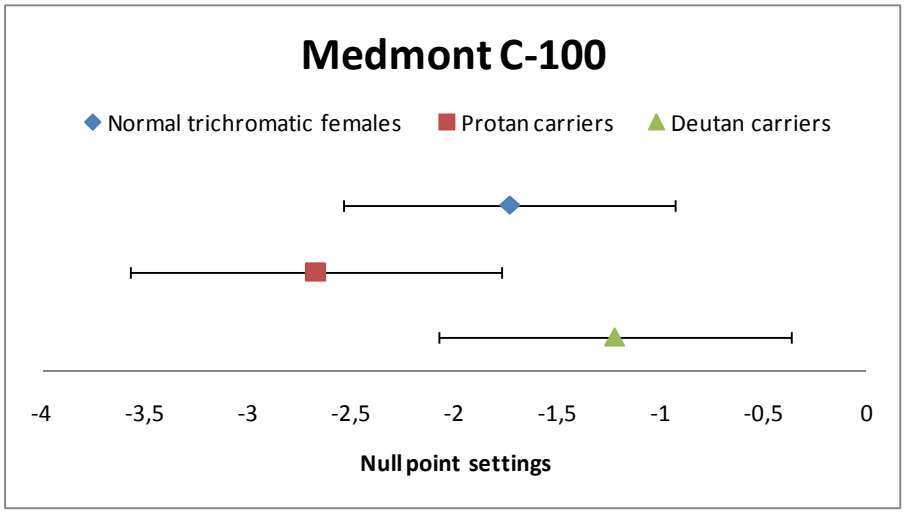

Figure 3-12 Medmont C-100: mean null-point and one standard error of mean presented for normal trichromatic females, protan carriers and deutan carriers (age is disregarded). The data are presented in different heights to show that they are overlapping.

Null-point settings for the normal trichromatic females ranged from -4.19 to +0.44, with a median setting of -1.81 and 95th percentiles that ranged from -3.84 to 0.31. The protan carriers' colour mixtures ranged from -3.88 to -1.44, with a median setting of -2.94, while the deutan carriers' colour mixture ranged from -2.94 to +0.25, with a median setting of -1.0. These results are presented in the form of a boxplot in Figure 3-13. 75% of protan carriers and 91% of deutan carriers set their null-points within the range of the normal trichromats' 95th percentiles.

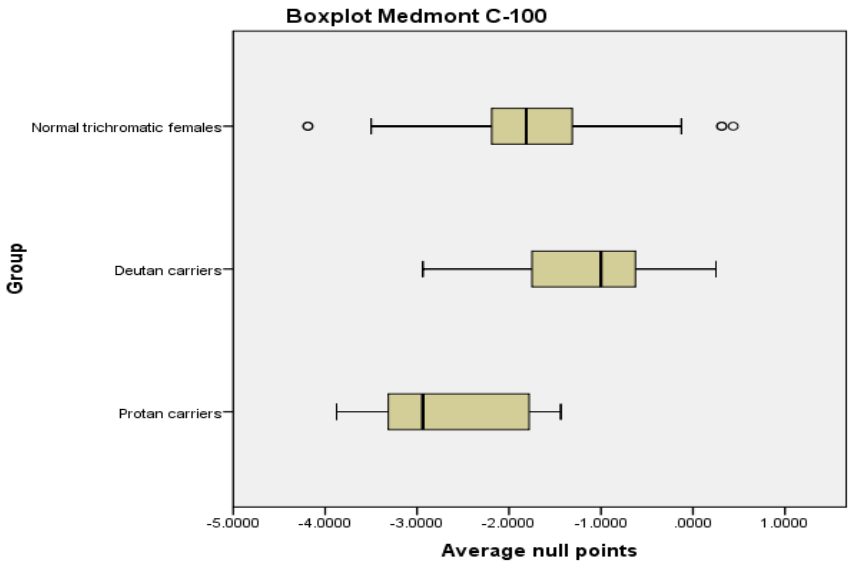

Figure 3-13 Medmont C-100: results presented in boxplots, showing median, upper and lower quartile, upper and lower adjacent value and outliers.

The null-points of the normal trichromatic females did not differ across the different age groups (ANOVA: f = 0.761, d.f. = 2, p = 0.47). A similar result was found for the protan carriers (ANOVA: f = 1.60, d.f. =2, p = 0.29). The deutan carriers aged 18-29 used significantly more red (that is, their null-points were more negative) compared to the other age groups of deutan carriers (ANOVA: f = 6.53, d.f. = 3, $p < 0.05$). This difference was still significant after Bonferroni correction. The data are presented in Figure 3-14.

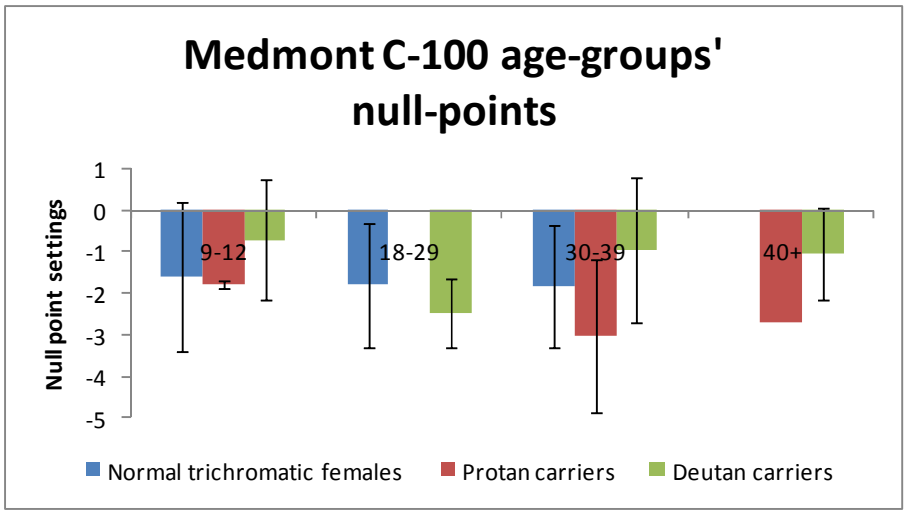

Figure 3-14 Medmont C-100: Null-points and 95th percentiles presented for the different age groups of normal trichromatic females, protan carriers and deutan carriers. The orientation of the figure differs from the other figures presenting data from Medmont C-100.

There was no significant difference in null-points between the normal trichromatic females, protan carriers and deutan carriers in either the 9-12 age group (ANOVA: f = 2.43, d.f. = 2, p = 0.101) or the 18-29 age group (ANOVA: f = 3.00, d.f. = 1, p = 0.09). However, there was a significant difference between protan and deutan carriers in the 30-39 age group (ANOVA: f = 7.11, d.f. =2, $p < 0.05$) and the over 40 age group, with protan carriers using, on average, more red in their null-points. The null-points of the normal trichromatic females were not significantly different from either the protan carriers or the deutan carriers in the two oldest age groups. The results are presented in Figure 3-14.

3.6 Colour deficient males

In the case of 21 of the 30 obligate carriers, the phenotypes of their colour deficient fathers or sons were established. Six colour deficient fathers and 15 colour deficient sons were tested. All the colour deficient males were classified as either protan or deutan deficient based on the results from the colour vision testing.

3.6.1 Questionnaire

The age of the 21 male subjects ranged from eight to 43 years, with a median age of 11.0 years and an average age of 18.86 (±13.92) years. All the colour deficient males tested in this study had previously had their colour vision tested and knew that they had a colour deficiency. They had a spherical-cylindrical equivalence of OD: -0.15 (±1.38) DS and OS: -0.17 (±1.40) DS. None of them had any systemic diseases or were taking any medicine that might affect their colour vision. They were all of Caucasian origin.

Twelve of the 21 colour deficient males reported problems in differentiating and discriminating different colours. Of these, two were protan deficient and the others were deutan deficient. Some had problems differentiating crayons; others had problems picking cowberries (mountain cranberry). Several of the deutan deficient males reported problems in differentiating blue and violet, orange and yellow, brown and red, brown and green, green and blue, green and grey and pink and violet. The protan deficient males reported problems differentiating yellow and light green colours and blue, violet and pink colours.

Seventeen of the colour deficient males were aware of a colour deficient relative. In 13 of these cases, the colour deficient relative was their maternal grandfather, in the other four cases it was either their brother or their maternal uncle.

3.6.2 Pseudoisochromatic tests

All the colour deficient males were tested with three different pseudoisochromatic plate tests (PIC-tests): the Ishihara 24 pl. Edition, the fourth edition of the Hardy-Rand-Rittler (HRR 2002) and the Neitz Test of Colour Vision (NTCV). Two of them were also tested with the CCT trivector and ellipse tests. The results are presented in Figure 3-15, Figure 3-16 and Figure 3-17.

Ishihara

All of the colour deficient males failed the Ishihara test (that is, they made three or more misreadings). Nineteen of them were classified as deutan deficient by the Ishihara test, while two remained unclassified. All of the males who were classified as protan by other colour vision tests were classified as deutan deficient by Ishihara. These subjects made, on average, 13.17 (±0.98) errors on the Ishihara, while those classified as deutan on other tests made, on average, 11.60 (±2.47) errors. In total, the colour deficient males, on average, made 12.05 (±2.25) errors on the Ishihara. The data are presented in Figure 3-15.

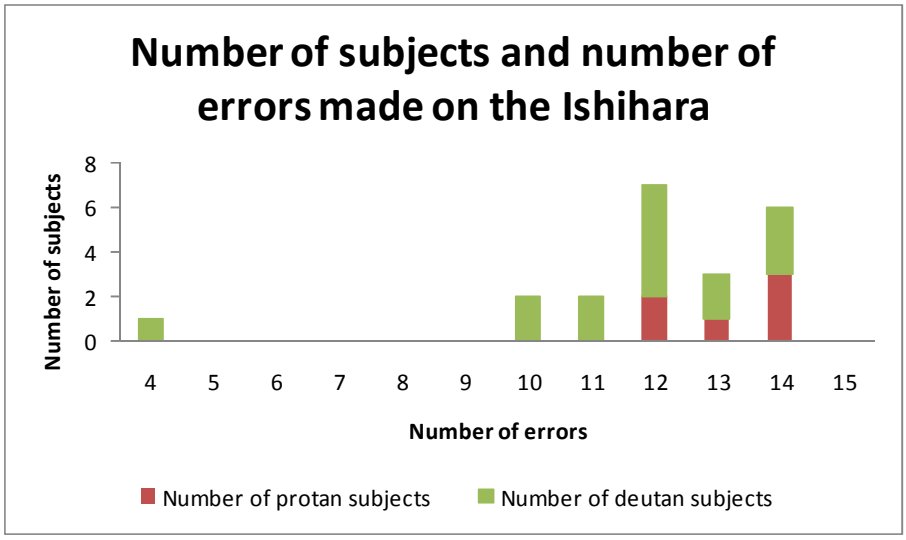

Figure 3-15 Distribution of subjects and number of errors made on the Ishihara of the colour deficient males (failing criteria: three or more misreadings).

HRR 2002

All the male subjects with abnormal colour vision made errors on the protan/deutan screening plates of HRR 2002. Out of the six symbols to be recognized on the red-green screening plates (plate seven to 10), the average number of errors on the protan/deutan screening plates was 5.19 (±0.93) (failing criteria: two or more misreadings on the screening plates). No subject made errors on any of the tritan plates.

Of the colour deficient males, the HRR 2002 test classified 14 to have a deutan deficiency, six to have a protan deficiency and one as a normal trichromat. Two of the 14 classified as deutan were graded as mild, four as medium and eight as having a strong degree of colour vision deficiency. Five of the protan deficient males were graded as medium colour deficient and one as mild. Of the six who were classified as protan deficient by the HRR 2002, only one was confirmed as such by the NTCV. The one classified as a normal trichromat by HRR 2002 was classified as having a mild deutan deficiency by the NTCV and was unclassified by the Ishihara test. These apparently conflicting results indicate a mild deficiency.

The Neitz Test of Colour Vision

All of the colour deficient males failed the NTCV test (that is, made one or more misreadings) and were therefore retested with another sheet of the test. Since all of them also failed the retest, none were classified as normal trichromats. Ten were classified as having abnormal red-green colour vision, but the test failed to classify them as either protan or deutan. Four were classified as deutan deficient, of whom one was classified as mild deutan, while the three others were classified as strong deutan deficient. Three were classified as strong protan deficient and four were unclassified (they mistook both blue-green and red-green plates). All of the colour deficient males failed test panel number nine (testing for mild deutan deficiencies), both on the first test and on the retest. On the retest, four had one or two fewer failures on the NTCV, while six made an error on one or more test panel. When tested the first time with NTCV, the colour deficient males made, on average, 4.9 (±1.30) mistakes. On the retest, they made, on average, 5.0 (±1.34) errors, see Figure 3-16.

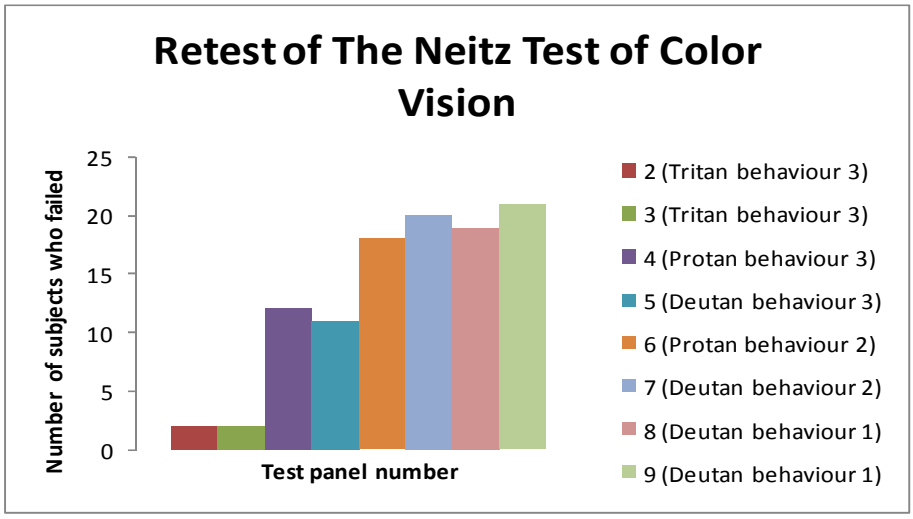

Figure 3-16 Distribution of colour deficient males who failed the different test panels on the NTCV when retested with a second sheet of the test (failing criteria: one or more misreadings).

CCT

Two of the colour deficient males (Figure 3-17) were tested with the CCT. Both were deutan deficient and exceeded the limits for both protan (545 and 595, respectively) and deutan (both 1100) axes on the CCT trivector test. Only one (#164) of them exceeded the limit of the tritan axis (198), while the other one (#037) exhibited normal values along the tritan axis (74). The data are presented in Figure 3-17.

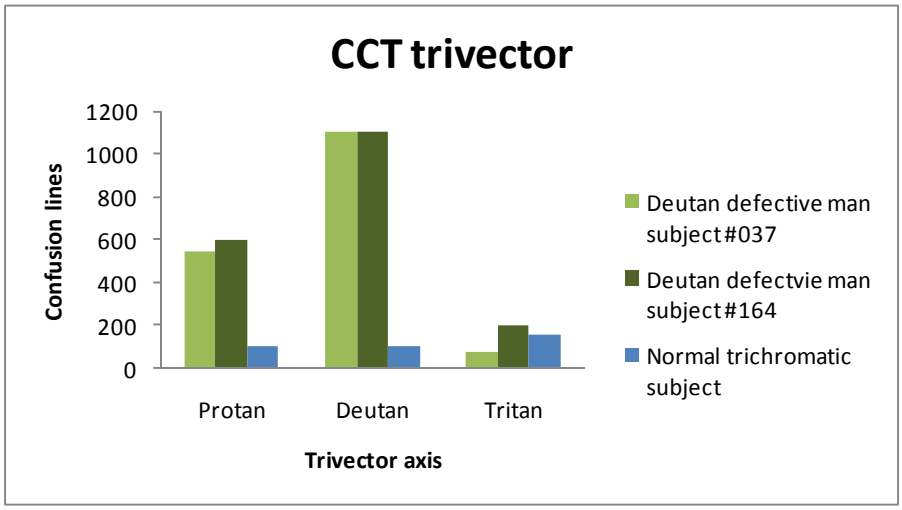

Figure 3-17 CCT trivector test results presented for the two colour deficient males (subjects with normal trichromatic colour vision are expected to perform below the limits 100 (protan), 100 (deutan) and 150 (tritan). The scale on the figure differs from that used in Figure 3-2.

Both subjects had approximately the same axis on the CCT ellipse test (168.9 (#037) and 172.3 (#164), respectively). The length of the ellipse and the axis ratio were significantly different, with #037 exhibiting larger values both for length and ratio (5.75 (#037) and 0.18 (#164) for length; 300.65 (#037) and 7.23 (#164) for axis ratio).

3.6.3 FM100-Hue

All the colour deficient males were tested with the FM100-Hue test. Almost 14% of them did not exceed the expected age-matched TES-value. The square root of total error scores (SQRT TES) were highest in the youngest age groups and then decreased with age. The data are presented in Figure 3-18, where the plot shows the distribution of square root TES, plotted against age, compared with expected square root TES scores for the different ages.

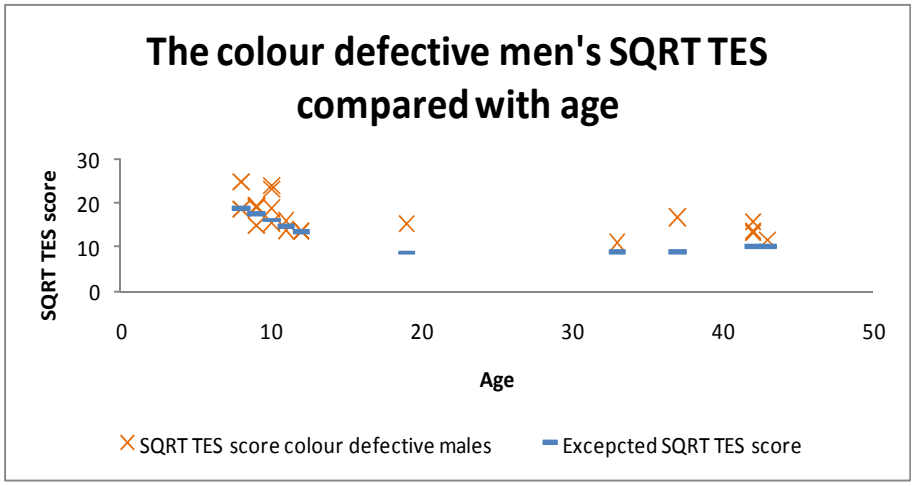

Figure 3-18 FM100-Hue: Distribution of square root TES for colour deficient males

Almost 17% of the protan deficient males had a mid-point indicating a protan defect, while 50% had a mid-point indicating a deutan deficiency; the rest could not be classified by the FM100-Hue test. Almost 75% of the deutan deficient males had a mid-point indicating a deutan deficiency, while the others were not classified by the FM100-Hue test. Around 71% of the colour deficient males were classified as red-green colour deficient by the FM100-Hue.

FM100-Hue		Confusion angle	Selectivity index	Confusion index
Protan deficient men	Mean	17,23	1,31	2,57
	1 SD	15,00	0,12	0,62
	Range min	-3,80	1,12	1,81
	Range max	38,50	1,43	3,68
Deutan deficient men	Mean	5,93	1,37	3,35
	1 SD	34,49	0,20	0,96
	Range min	-49,70	1,04	1,74
	Range max	75,10	1,73	4,69

Table 8 FM100-Hue: Confusion angle, selectivity index and confusion index presented for protan and deutan deficient males.

3.6.4 Anomaloscopy

Rayleigh match

Six colour deficient men, aged 33-43, were tested with Rayleigh match anomaloscopy. Five were classified as deutan deficient, three as deuteranomalous and one as a deuteranope. The deuteranomalous man had a mean matching midpoint of 19.93 (±2.60), a mean matching range of 18.95 (±18.20) on the Rayleigh match and set matching luminance to 14.14 (±1.14). The deuteranope had a matching midpoint of 36.50, a matching range of 73 and set matching luminance to 14.40. One was classified as protan deficient (protanomalous), he had a matching midpoint of 53.5 and a matching range of 27. Compared with the deutan deficient men and the normal trichromatic females, the protan deficient man set a lower matching luminance, with a value of 9.45. The data are presented in Figure 3-19.

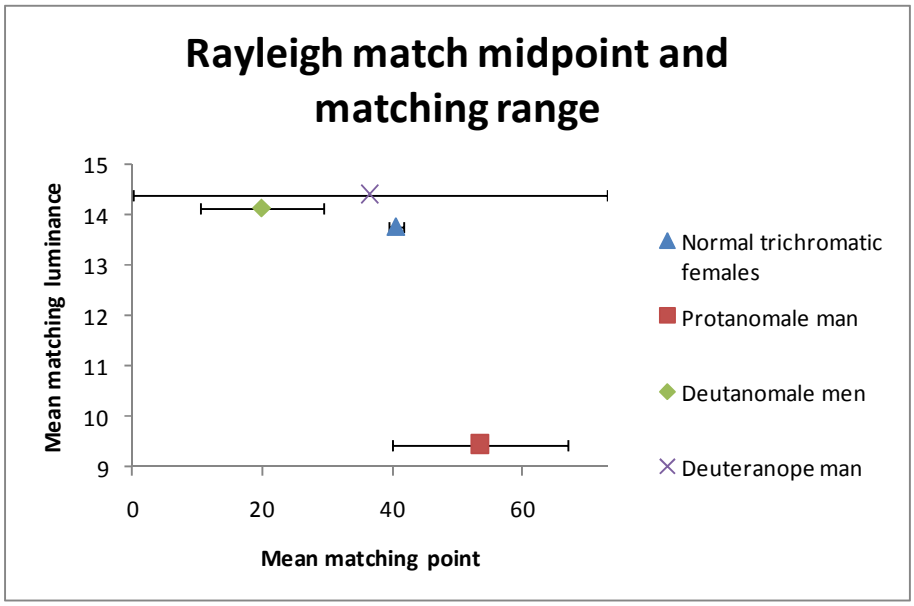

Figure 3-19 Rayleigh match midpoint and mean matching luminance presented for colour deficient men. The scale on the figure differs from that used in Figure 3-6. The error bars represent matching range.

The results of the HRR 2002 test correspond closely with the results from the Rayleigh match, and the relationship between Rayleigh matching range and HRR classification is significant (Student-t: t = 7.59, d.f. = 4, $p < 0.001$). The results are presented in Table 9. Only the HRR 2002 results were compared to the Rayleigh match, because both the Ishihara and NTCV tests classified the colour deficient males differently to the anomaloscope test.

HRR classification	Number	Mean matching range	SD matching range
Protan medium	1	27,00	-
Deutan mild	2	6,30	1,06
Deutan strong	3	45,40	27,35

Table 9 Classifications and grading of HRR 2002 and the subjects' mean matching ranges on the Rayleigh match.

Moreland match

Six colour deficient men, aged 33-43, were tested with Moreland match anomaloscopy. Five of the men were classified by the Rayleigh match as deutan deficient, three as deuteranomalous and one as a deuteranope. The deutan deficient men had a mean matching midpoint of 43.43 (±7.04) and a mean matching range of 20.38 (±11.92) on the

Moreland match. They set matching luminance, on average, to 39.41 (±3.75). One man was classified as protan deficient (protanomalous) by the Rayleigh match. On the Moreland match he had a matching midpoint of 48.65, a matching range of 3.90 and set the matching luminance to a value of 42.00. There was a significant difference (ANOVA: f = 12.97, 12.48 and 7.80, d.f. = 2, $p < 0.05$) between the normal trichromatic females and the deutan and protan deficient males for the Moreland match midpoint, matching range and matching luminance, but not between deutan and protan deficient men (ANOVA: f = 1.59, 0.46 and 0.40, d.f. = 1, $p = 0.26$, 0.54 and 0.56). The data are presented in Figure 3-20.

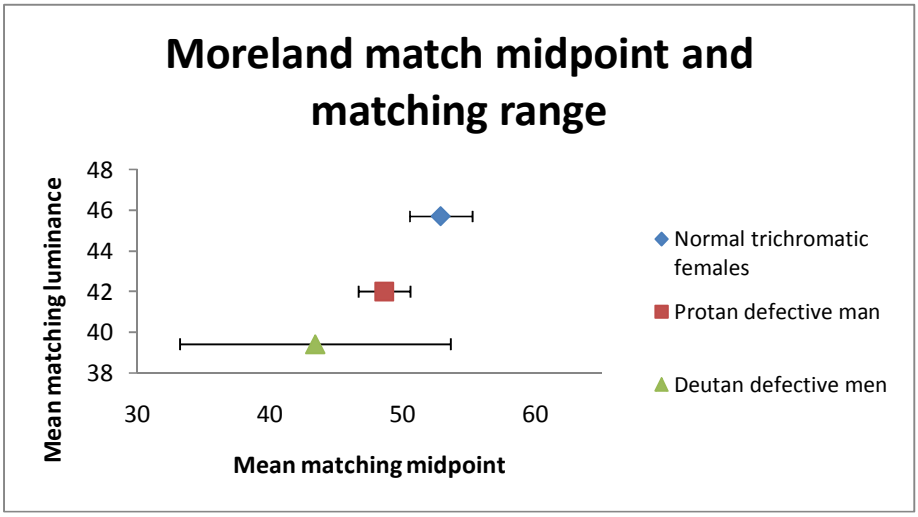

Figure 3-20 Moreland match mean midpoint and mean matching luminance presented for colour deficient men. The y-scale on the figure differs from that used in Figure 3-9 and Figure 3-10. The error bars represent mean matching range.

3.6.5 Medmont C-100

As Figure 3-21 shows, the colour deficient males were all classified correctly as either protan or deutan deficient by the Medmont C-100 colour vision test. The protan deficient males used more red in their colour mixtures, with an average setting of -4.22 (±0.25), a median of -4.13 and a range of -5.0 to -3.31. The deutan deficient males used more green in their colour mixtures, with an average value of 0.41 (±0.35), a median of 0.25 and a range of -1.56 to +4.56. The average settings made by the deutan deficient males had a greater spread than the settings made by the protan deficient males. The difference in null-points between protan and deutan carriers was significant (ANOVA: f = 62.73, d.f. = 1, $p < 0.05$).

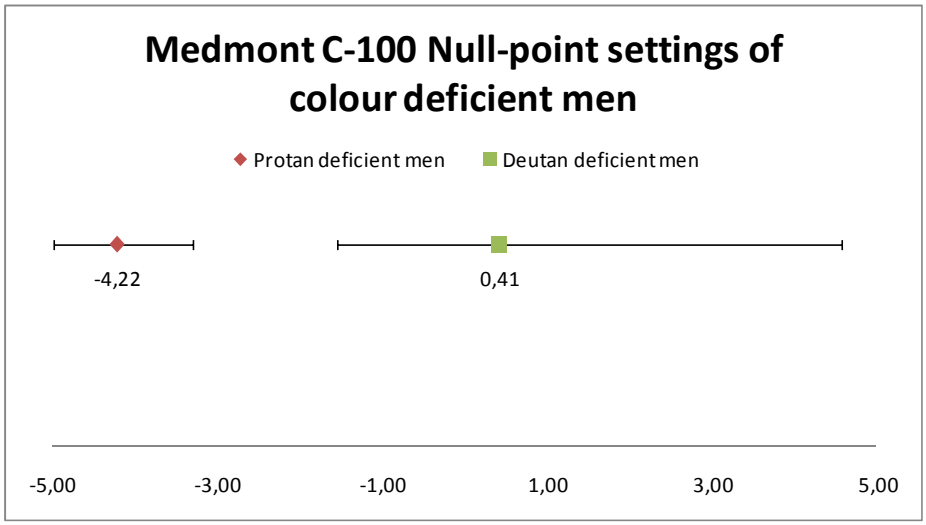

Figure 3-21 Average settings and range for the Medmont C-100 test, presented for protan and deutan deficient males. The scale on the figure differs from that used in Figure 3-12

The HRR 2002 and Medmont C-100 tests both classified the same male subjects as either protan or deutan, except for one male who was classified as a normal trichromat by the HRR 2002 and as a deutan by the Medmont C-100.

4 Discussion

4.1 Colour vision of carriers is impaired when compared to normal trichromats

In this study, protan and deutan carriers performed worse than their normal trichromatic peers when assessed with colour vision tests such as the Ishihara, HRR 2002, NTCV and FM100-Hue. The carriers made more errors and some displayed impaired colour vision. The difference between carriers and normal trichromatic females was most prominent in the youngest age group (9-12 years).

All the carriers in this study were known, obligate carriers, since the status as a carrier is inferred from the status of the colour vision of her son/father, measured either by the questionnaire or by colour vision testing.

Hill et al. (1982) proposed that children, both those with normal trichromatic colour vision and those with colour vision deficiencies, should perform worse than adults on colour vision tests. Very few studies, however, have examined how girls perform on standard colour vision tests (for a review see Ref. Baraas, 2008), and no studies have evaluated how young carriers perform on the same colour vision tests. The results from this study show that young girls, in general, exhibit higher error scores (Figure 3-3) and fail more tests than older participants (Figure 3-1). Moreover, the poorest performance was observed in the youngest carriers.

Both carriers and normal trichromatic females are expected to fail some colour vision tests, although carriers are expected to fail more often (Hill, 1980, Krill and Schneiderman, 1964). Verriest (1972) showed that 15.5% of heterozygotic adult carriers scored worse than genotypically normal subjects, on various colour vision tests, hence, carriers often show slight to moderate colour vision deficiencies, particularly on the Ishihara and other PIC-tests (e.g. Waaler, 1927, Crone, 1959, Waaler, 1967, Hill, 1980, Jordan and Mollon, 1993b). The results of the current study are in agreement with these prior observations, since carriers failed both the FM100-Hue and PIC-tests more frequently than did their normal trichromatic peers (Figure 3-1, Table 3, Table 5 and Table 7).

Cosstick and colleagues (2005) reported that 13.1% of normal trichromatic subjects (both sexes, aged 6 years) made more than three errors on the Ishihara test, although they did not state whether any of their female participants were carriers. In the current study, normal trichromatic females in the 9-12 year old age group produced fewer misreadings (Table 4) than the participants in the Cosstick et al. (2005) study. These subjects were between three and six years older than those in the Cosstick et al. (2005) study, hence our results support the idea that in children, colour discrimination improves with age. The deutan carriers in the current study, however, were four times more likely than their normal trichromatic peers to make more than three misreadings on the Ishihara test. If Cosstick et al. (2005) unknowingly included some carriers in their 'normal' trichromat group, then irrespective of the age differences between the subjects in the two studies, the proportion of participants who made three or more misreadings would be expected to be higher than if only non-carrier normal trichromatic females had participated. It is not possible, therefore, to conclude that the different results obtained by these two studies were due entirely to effect of age on colour discrimination ability.

All subjects who misread one or more plates on the HRR 2002 test, misread plate seven (the most desaturated plate on HRR 2002 (Dain, 2004b)) and the proportion of subjects who failed this plate was lower when retested (3.2.1). Carriers made more errors than their normal trichromatic peers, both when tested for the first time and when retested. An earlier study has reported that a deutan carrier made an error on plate seven (Bailey et al., 2004). This is consistent with the results from the current study, where both protan and deutan carriers failed plate seven more often than their normal trichromatic peers.

It is known that incidence of errors on the FM100-Hue test changes with age for normal trichromatic females (Kinnear and Sahraie, 2002, Verriest et al., 1982). This notion is supported by the current result, which showed that FM100-Hue error scores for normal trichromatic females followed a U-shaped function when plotted against age. Moreover, a similar U-shape function was observed in the error scores of the obligate carriers' (Figure 3-4).

If the youngest age group is disregarded, twice as many carriers as the normal trichromatic females exceeded a total error score of 100 when tested with FM100-Hue. Some studies have found that adult carriers perform worse on the FM100-Hue test than normal

trichromatic females (Hill, 1980, Krill and Schneiderman, 1964, Verriest, 1972), whilst others have found no difference (Jordan and Mollon, 1993b). The results from the current study imply that obligate carriers (in the age groups 18-29 and 30-39), exhibit a higher square root TES than their normal trichromatic peers (Figure 3-3 and Table 7). The current study, therefore supports to some extend other studies (Hill, 1980, Krill and Schneiderman, 1964, Verriest, 1972) that suggest that carriers perform worse on this test, and the adult carriers' performance when tested on the FM100-Hue test was, therefore, on average poorer, but not statistically significant poorer, compared with their normal trichromatic peers.

The results from PIC-tests and FM100-Hue imply that the carriers' colour vision is poorer when tested with PIC-tests and FM100-Hue compared with their normal trichromatic peers, and that obligate carriers show reduced colour discrimination when tested with these tests. Since children understand the concept of seriation, as shown by tests with varying grey levels (Dain and Ling, 2009), the variability in the 9 to 12 age group's error score when tested with the FM100-Hue could be related to variations in maturation of visual discrimination skills (Table 7). Maturation of visual function occurs over different ages in different children (Norcia and Manny, 2003) and this may have influence on a child's performance when colour vision is tested. Testing can be perceptually and cognitively challenging for children and this is reflected in the results of the current study. Compared with adults, children have higher error scores on colour vision tests (Hill et al., 1982, Lakowski, 1969a). This is reflected in the current results from both the FM100-Hue and PIC-tests.

It has been previously reported that colour vision in deutan carriers is poorer than in either protan carriers or normal observers (Hood et al., 2006). This is probably due to the extreme L to M-cone ratio found in deutan carriers, since it is known that the more asymmetrical the L to M-cone ratio is, the poorer is the subject's chromatic contrast sensitivity (Hood et al., 2006). The presence of Ser on residue 180 of the L-pigment may also be a contributing factor. The results from the current study are compatible with the Hood et al. (2006) findings, since deutan carriers showed poorer performance than protan carriers on both the PIC-tests and the FM100-Hue test.

4.2 Reduced sensitivity in the medium and long wavelength regions

Deutan carriers required on average more green and protan carriers more red on both the Rayleigh match (Figure 3-6) and the Medmont C-100 (Figure 3-12 and Figure 3-13) compared with the normal trichromatic females. However, this difference was significant only on Rayleigh match midpoints between deutan- and protan carriers, and deutan carriers and their normal trichromatic peers. There was no significant difference in Medmont C-100 null-point settings between the three groups.

It has previously been reported that adult carriers exhibit a shift in Nagel match midpoint and an enlarged Nagel matching range (Krill and Schneiderman, 1964, Hill, 1980) and that they do not accept the setting of the normal equation (Linksz, 1964a). The carriers in the current study exhibited a shift in Rayleigh match midpoints, with protan carriers on average using more red and deutan carriers more green (Figure 3-6). As a trend, protan carriers also exhibited, on average, a larger matching range compared with their normal trichromatic peers and deutan carriers and showed therefore, on average, poorer colour discrimination (3.4.1). However, the difference in matching ranges between the three groups was not statistically significant. When testing a female subject, without knowing whether she was a carrier, only carriers of deutan deficiencies could be distinguished from the normal trichromatic females for certain since they exhibited a significantly different match midpoint, when compared with their normal trichromatic peers. Since protan carriers exhibit a shift in the Rayleigh match and on average an enlarged matching range, it might be possible to distinguish them from normal trichromatic subjects, but the diagnosis as a protan carrier would be more unreliable. The results also imply that it might be possible to identify a known obligate carrier as either a protan or deutan carrier without any knowledge about her father's colour vision deficiency, based on the results from Rayleigh anomaloscopy.

Rayleigh anomaloscopy is often used as a gold standard or a point of reference for other clinical tests (e.g. Squire et al., 2005, Lakowski, 1969b, Bailey et al., 2004, Dain, 1998). However, subjects classified with poor colour discrimination by the FM100-Hue did not have a larger matching range than the subjects classified as normal trichromats (Figure 3-7). This implies that the results from FM100-Hue do not correlate well with the results from the Rayleigh match. This is confirmed by a recent study performed by Baraas et al. (2010),

that showed that the anomaloscope does not predict performance in more general colour judgments and that the degree of colour constancy was unrelated to both match midpoints and matching ranges.

Normal trichromatic subjects who perform the Medmont C-100 test are expected to have their null-points between -1 and +1 (or, in rare cases, -2 to +2) (Harris and Cole, 2005a), with an average setting of zero. The normal trichromatic females in the current study did not all fall within these limits, in fact only 15% of them set their null-points between -1 and +1. This implies that a new range of expected null-points might be needed for the Medmont C-100 test. The current results suggest that a range of -4.19 to +0.44 (mean -1.73 (±0.81)) would be more appropriate. It is possible, however, that null-points can be different (shifted) in different Medmont C-100 devices (Figure 3-11). Two previous studies (Harris and Cole, 2005a, Harris and Cole, 2005b) only included carriers and colour deficient participants and assumed that settings outside -1 and +1 were abnormal readings. It is, therefore, difficult to compare the null-points set by normal trichromats with the results of these two studies. Another study did, however, include normal trichromats (both sexes) (Robbins, 2005) and concluded that the null-points of a normal trichromat would be from -0.64 to +1.09. This does not coincide with the results from the current study. This may imply that there is a difference between the null points of normal trichromatic females and those of normal trichromatic men. The degree of variability in normal trichromats' null-point settings seen in the current study has previous been reported by Metha and Vingrys (1992), who found that colour deficient subjects showed less variability and were more precise in their settings, than their normal trichromatic peers, when tested with the Medmont C-100.

Even though both the protan and deutan carriers had shifted null-points to some degree, compared with the normal trichromatic females, when tested with Medmont C-100, the difference was not significant. 75% of protan carriers and 91% of deutan carriers set their null-points within the normal trichromats' 95th percentiles, hence, the Medmont C-100 could not conclusively identify either protan or deutan carriers.

The reduced sensitivity for long and medium wavelengths of carriers has been reported in previous studies (Hood et al., 2006, Jordan and Mollon, 1993b, Crone, 1959) and is often referred to as Schmidt's (Schmidt, 1934, Hood et al., 2006, Jordan and Mollon, 1993b) or de

Vries' sign (De Vries, 1948, Jordan and Mollon, 1997). It is claimed that the Medmont C-100 is able to identify female carriers of protan and deutan deficiencies.

Deutan carriers fell within normal limits on Medmont C-100, but, as previously reported by Crone (1959), they used, on average, more green in their colour mixtures and showed, on average, a reduced sensitivity in the short wavelength region of the relative luminous efficiency curve. Unlike deutan carriers, protan carriers were more sensitive to green light and they used, therefore, on average, more red in their colour mixtures and hence, showed a reduced sensitivity in the long wavelength region. This is comparable to the results from Rayleigh match midpoints (3.4.1). Since this difference in null-points between protan and deutan carriers and their normal trichromatic peers was not significant, either when age was disregarded or when the different age groups were compared, neither Schmidt's nor de Vries' sign was definitively demonstrated by the Medmont C-100 test. Hence, the Medmont C-100 test failed to identify protan and deutan carriers among the normal trichromatic females and the null-points of the three groups overlapped considerably (Figure 3-12 and Figure 3-13).

The deutan carriers aged 18-29 years used significantly more red (that is, their null-point values were more negative) compared with the other age groups of deutan carriers. This result supports the notion that the Medmont C-100 test is not able to distinguish protan and deutan carriers, since the deutan carriers in this age group set their null-points towards what is expected for a protan carrier (Harris and Cole, 2005a, Harris and Cole, 2005b).

There was a statistically significant difference in null-point settings between protan and deutan carriers in the age groups 30-39 years and 40 years and older, where the protan carriers used more red (that is, their null-point values were more negative) and deutan carriers more green (that is, their null-point values were more positive) (see 3.5). This implies that the test might be able to differentiate carriers in these age groups. Note that the settings of the carriers were not significantly different from their normal trichromatic peers. This implies that the Medmont C-100 test might be able to identify known carriers, aged 30 years and older, as either protan or deutan carriers. Since the difference in null-point settings between deutan and protan carriers (aged 30 and older) was significant, both Schmidt's and de Vries' signs were observed. This finding is in accord with previous studies

that have shown reduced sensitivity in carriers for long and medium wavelengths (Hood et al., 2006, Jordan and Mollon, 1993b, Crone, 1959).

Several of the participants reported that the Medmont C-100 test was difficult to perform and specifically, that the minimum sensation or cessation of flicker was hard to find. This probably explains the relatively high level of variance in null-point settings set by the normal trichromatic females. This may also explain why the difference in null-point settings was only statistically significant between carriers aged 30 years and above. It is possible that the test was too difficult for the children and young adults in this study to perform (both the normal trichromatic females and the carriers), hence it is possible that the null-point settings of the two youngest groups were not reliable.

The shifts in Rayleigh match midpoint and Medmont C-100 null-points seen in this study might be due to the mosaic of normal and defective patches in the retina, that are known to exist in carriers (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964). This retinal mosaic can vary from predominantly normal to predominantly defective, due to random X-inactivation (Lang and Good, 2001). Based on a carrier's phenotype and genotype, she is expected to have an altered L to M ratio (Hofer et al., 2005). This may lead to misjudgements of the colour appearance of tiny objects (Roorda and Williams, 1999) and to a shift in the midpoint/null-points in Rayleigh match and Medmont C-100 tests. This accords well with the results of the current study. Colour-space compression in a red-green dimension and reduced salience of that dimension is often seen in heterozygous women (Bimler and Kirkland, 2009), in line with the results of this study.

The observed shift in Rayleigh match midpoints and Medmont C-100 null-points may also be explained by Ser/Ala polymorphism, (see 1.4.2 and 1.6.4) which may cause small variations in the absorption maxima of visual pigments (Winderickx et al., 1992). The carriers in the current study exhibited a shift in Rayleigh match midpoint and would, therefore, not accept the setting of the normal equation. The presence of Ser at residue 180 of the L-pigment increases sensitivity to red light (Winderickx et al., 1992, Sharpe et al., 1999) and might explain why the deutan carriers set their match midpoints and null-points towards the green region. Conversely, the protan carriers' shift to the red region may be explained by the presence of Ala that results in a shift to longer wavelengths (Sharpe et al., 1998, Merbs and Nathans, 1992, Asejno et al., 1994).

4.3 Performance of colour deficient males on colour vision tests

In the case of 21 of the 30 obligate carriers, the phenotypes of their colour deficient fathers or sons were established. With a battery of different colour vision tests, the males in this study was classified as either protan (n = 7) or deutan (n = 15) deficient. Of the men tested with the anomaloscope on the Rayleigh match, one was classified as deuteranope. Twelve of the 21 colour deficient male participants in the current study reported that they had problems differentiating and discriminating different colours. Specifically, they reported problems distinguishing between different pastel colours and also between colours such as olive green and brown, which is in line with previous findings (Neitz and Neitz, 2000).

The males were classified as colour deficient by the different PIC-tests, but the results from the different tests were not always commensurate with each other. As seen in Figure 3-15, all the colour deficient males made more misreadings than expected for a normal trichromatic person on the Ishihara test. Even though it has been claimed that the Ishihara can classify both protan and deutan deficiencies (Birch, 1993), this was not the case in the current study, where 19 of the colour deficient males were classified as deutan deficient by the Ishihara test, none were classified as protan deficient and two remained unclassified. Only one man made less than nine misreading on the tests, which indicates a mild colour vision deficiency.

The HRR 2002 test was able to classify and grade 20 of the 21 colour deficient males. As expected (Bailey et al., 2004), the results of this test corresponded well with what was determined by the anomaloscope (Table 9). When comparing the results from HRR 2002 with the other colour vision tests, the test succeeded in classifying the males as either protan or deutan deficient, and none were classified as having a tritan deficiency.

All the colour deficient males failed the NTCV-test. The test was not, however, able to determine correctly in all cases whether the deficiency subtype was protan or deutan. The colour deficient males failed, on average, the same number of test panels both first time they were tested and also when retested with another sheet of NTCV. This shows that the test has good repeatability. Neitz and Neitz (2001) have claimed that the test is able to detect colour deficient subjects and that was the case in the current study. The colour deficient males most often failed the most desaturated plates (six, seven, eight and nine,

protan and deutan behaviour 1 and 2) (Figure 3-16) which are the most difficult to discriminate for colour deficient subjects. However, the NTCV was not able to classify this study's males as either protan or deutan deficient and the results were not compatible with the results from either Ishihara or HRR 2002

Two deutan deficient men were tested with the CCT Trivector test. As in a previous study (Mollon and Regan, 2000), the test classified them both correctly as deutan deficient and both men also exceeded the normal limits on the protan and deutan axes (Figure 3-17). Both men ended with approximately the same axis on the CCT ellipse test. These axes correspond to the red-green axis and classify both men as deutan deficient. The length of the ellipse and the axis ratio were significantly different, and #037 exhibited larger values both on length and ratio. This result shows that #037 has a stronger grade of the deutan colour vision deficiency compared with #164.

All colour deficient males were tested with the FM100-Hue test. As seen with the normal trichromatic females in this study, the SQRT TES scores were highest in the youngest age groups and decreased with age, in agreement with Kinnear and Sahraie (2002). Almost 14% of the colour deficient males did not exceed the expected age matched TES-value limit (Figure 3-18). This could imply that even though the colour deficient males had impaired colour discrimination, they might have been highly motivated to do well and were trying hard to do the test as correctly as possible. This might result in a larger number of caps being mistaken around the area where the red-green axis is, rather than in the area where the blue-green axis is. These results can be explained by the fact that both normal observers and colour deficient subjects may have good or poor colour discrimination (Farnsworth, 1957), which is reflected by the amount of colour deficient males who did not exceed the upper age expected TES-limit in this study. The high confusion index value achieved by both protan and deutan deficient males shows that they have a higher degree of colour vision loss when compared to the obligate carriers (Table 6 and Table 8).

The FM100-Hue test did not correctly identify all the deficient males as either protan or deutan, as it was expected to do (Farnsworth, 1957). However, about three quarters of the colour deficient males were classified as red-green colour deficient. This shows that the FM100-Hue distinguished between two important axes in colour space - the red-green axis, involving changes in L- and M-cone excitation and the tritan axis, involving changes in S-

cone excitation (Knight et al., 1998). The dichromatic confusion lines of FM100-Hue tend to orientate themselves at different angles, with an average protan locus being about 17.23° and an average deutan locus to 5.93° (Table 8). This correlates with the results of Vingrys and King-Smith (1988), who found that the protan axis tended to be a higher angle than the deutan axis. However, in the current study both the protan and deutan deficient males exhibited higher values for the angles than the colour deficient males in Vingrys and King-Smith's (1988) study. Overall, the FM100-Hue test identified more of the protan deficient males than the Ishihara and, as previously reported (Lakowski, 1969b), it was therefore more accurate in identifying protan deficient males.

When a colour deficient subject is tested with Rayleigh anomaloscopy, the proportion of red and green will vary according to the type of deficiency. For example, a protanomalous person will require more red, whilst a deuteranomalous person will require more green (Lakowski, 1969b, Ventura et al., 2003, Neitz et al., 1996, Linksz, 1964a). Our results were largely compatible with these earlier findings. The men's Rayleigh match midpoint and matching range varied according to the type of deficiency (Figure 3-19). Furthermore, the more severe the deficiency classified by HRR 2002, the larger was the Rayleigh matching range (Table 9). This relationship was significant, which implies that the results from HRR 2002 corresponded well with the results from the Rayleigh match. As expected (Merbs and Nathans, 1992), none of the deutan deficient men made the same colour matches when tested with Rayleigh anomaloscopy. This is thought to be due to polymorphism in the L-pigment, where the absorption maxima differ subtly from the others in its spectral position (Merbs and Nathans, 1992, Deeb, 2006).

The Medmont C-100 test has been claimed to categorize protan and deutan deficiencies seemingly without error (Cole et al., 2006, Harris and Cole, 2005a) and it is, therefore, often administrated only to subjects who have already failed other colour vision tests, in order to classify their colour deficiency (Metha and Vingrys, 1992). The results from the current study are compatible with this claim, in that the colour deficient males were successfully classified as either protan or deutan by the Medmont C-100 test. Protan deficient males are expected to set their null-point between -2 and -5, while deutan deficient males set theirs between +2 and +5 (Harris and Cole, 2005a). Null-points for the protan deficient males in the current study ranged from -5.0 to -3.31; for the deutan deficient males null-points ranged from -1.56 to +4.56 (Figure 3-21). The protan deficient males' range of null-point

was within expected values, while the deutan deficient males exceeded the limits of expected null-points. This means that the null-point of deutan deficient males was shifted for the specific Medmont C-100 device used and the deutan deficient males used more red than expected in their null-point setting. In any case, the null-points of protan and deutan deficient males did not overlap and all the colour deficient males were correctly classified by the Medmont C-100 test. As previously suggested (Harris and Cole, 2005a), the Medmont C-100 might therefore be an effective and accurate test to classify subjects who have failed other colour vision tests, but it is not ideal as a screening test for colour vision deficiencies. The results from Medmont C-100 corresponded well with the results from the HRR 2002, in that the two tests classified the same males as either protan or deutan deficient, hence, both tests worked properly to classify colour deficient subjects.

4.4 Carriers vs. colour deficient fathers and sons

The high percentage of deutan carriers who failed one or more of the plates that detect deutan deficiencies on the NTCV test implies that deutan carriers made the same errors as their colour deficient fathers/sons and that NTCV may detect some deutan carriers as well as mild deuteranomalous males. Some studies have shown that a carrier partly shares her father's/son's colour vision deficiency (Krill and Schneiderman, 1964, Rodríguez-Carmona et al., 2008). The results from the current study support this idea; the deutan carriers failed the NTCV test more often than the other PIC-tests (Table 3). Of the deutan carriers who failed the NTCV test, 86% failed plate nine (the most desaturated plate, deutan behaviour 1). This might be due to the sensitivity in plate nine, which almost all who failed NTCV mistook. This plate is one of the two most desaturated red-green panels (Neitz and Neitz, 2001) and might therefore be difficult to discriminate, not just for colour deficient subjects, but also for normal trichromatic females and carriers. This has previously been discussed by Baraas (2008), who reported that female participants showed poorer performance than expected when tested with NTCV. No other report has been found that describes how young girls perform on NTCV. For a subject with normal trichromatic vision, both the grey-scale and coloured symbols might be difficult to detect and they appear equally visible. This might be confusing for the observer and might lead them to mark out the grey-scaled symbol even though they saw the coloured symbol as well.

The obligatory carriers produced larger values on the CCT trivector test on both the protan and the deutan axes (Figure 3-2) compared with their normal trichromatic peers. This difference was statistically significant. Hence, carriers showed reduced sensitivity in both the medium and the long wavelength region of the luminous efficiency curve. Since the carrier's retina consists of a mosaic of both normal and defective patches (Jordan and Mollon, 1993b, Krill and Schneiderman, 1964), her colour vision may vary from predominantly normal to predominantly defective (Lang and Good, 2001). This may explain why the carriers in this study achieved higher error scores on the red-green axis, as would be expected from their colour deficient fathers/sons. Regan et al. (1994) described a protan carrier who, on average, exhibited ellipses on the CCT Ellipse test that were oriented at a lower angle than those of the normal trichromatic observers. Conversely, in the current study the carriers, on average, exhibited ellipses that were oriented at a higher angle compared with to their normal trichromatic peers. Taken together, the results from Regan et al. (1994) and the current study imply that carriers do not show any specific angle when tested with the CCT ellipse test.

When tested with Rayleigh anomaloscopy, the protan carriers set matching luminance below that of the normal trichromats and the deutan carriers (Figure 3-6), which might imply that they set their matching luminance towards where their colour deficient father/son would be expected to set their matching luminance. This was also the case for the deutan carriers, who on average used more light in their matching luminance compared to their normal trichromatic peers. Since there was no significant difference in matching luminance between either the normal trichromatic females and the deutan carriers or the protan carriers and their peers, the Oculus anomaloscope was not able to distinguish carriers from normal trichromatic subjects, based only on matching luminance. The results do, however, imply that the Oculus anomaloscope can distinguish known obligate carriers as either protan or deutan, based both on match midpoints, matching luminance and matching ranges.

The deutan deficient men had larger matching ranges than the normal trichromatic females, while the protan deficient men had a smaller matching range, when tested with Moreland anomaloscopy (Figure 3-20). This is largely compatible with the results of the female carriers, where the deutan carriers showed, on average, poorer performance on the Moreland match (Figure 3-9 and Figure 3-10). These carriers also had an enlarged matching

range compared with both the protan carriers and their normal trichromatic peers. Both the carriers and colour deficient men set matching luminance, on average, below that of the normal trichromatic females. These results imply that both carriers of deutan deficiencies and deutan deficient men show poorer performance on the Moreland match and that, in addition to reduced sensitivity to medium wavelength light, they also show, on average, reduced sensitivity to short wavelength light.

5 Concluding remarks

Both protan and deutan carriers in this study performed worse on colour vision tests than their normal trichromatic peers. Carriers failed the tests more often and showed impaired colour vision. The difference between carriers and normal trichromatic females was most prominent in the youngest age group (9-12 years), where the carriers failed significantly more colour vision tests. On both the PIC-tests and the FM100-Hue, the youngest carriers scored worse than the older carriers. A similar improvement in colour discrimination with age was also observed in normal trichromats. This indicates that visual discrimination skills, such as the discrimination of colour, improve through adolescence.

The results imply that some young female carriers may have exacerbated problems with colour discrimination due to the combined effects of being a carrier and having an immature visual system. These girls may confuse colours during their early years at school. Due to the carriers' poor performance on PIC-tests, it is important to screen for impaired colour vision at an early age. Screening for impaired colour vision is not part of the Norwegian Directorate of Health's recommended directions for screening children's vision (SHDIR, 2009). This can cause impaired colour vision to remain undetected.

Compared with the normal trichromatic females, deutan carriers required, on average, more green and protan carriers more red, on both the Rayleigh match and the Medmont C-100, showing therefore, a reduced sensitivity in the medium and long wavelength regions. The results imply that it may be possible to identify known obligate carriers as either protan or deutan, based on the Rayleigh anomaloscope and Medmont C-100 settings.

Deutan carriers scored significantly worse on the colour vision tests used in this study, confirming that they have poorer colour vision than protan carriers.

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7 Appendix A-J

Appendix A

Letter of reply from REK

Letter of reply from Data Inspectorate

Appendix B

Research protocol

Appendix C

Agreement with Bø municipality

Agreement with Notodden municipality

Agreement with Kongsberg municipality

Appendix D

Informed written consent

Appendix E

Questionnaire parents/superior

Questionnaire female optometry students

Appendix F

Scoring sheet

Appendix G

Information letter to rectors

Information letter to normal trichromatic girls

Information letter to colour deficient boys, Notodden and Bø

Information letter to colour deficient boys, Kongsberg

Information letter to carriers

Appendix H

Variables colour vision

Variables questionnaire

Appendix I

Moreland match midpoints

Appendix J

The carriers' individual scores on the different tests

Appendix A

Letter of reply from REK

UNIVERSITETET I OSLO
DET MEDISINSKE FAKULTET

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Dato: 5.6.09
Deres ref.:
Vår ref.: S-08155a; S-06436a: S-05388

S-08155a Spatial synsfunksjon hos mennesker med normalt og svekket fargesyn: Interaksjon mellom staver og tapper, samt betydningen av genotype versus fenotype [6.2008.499]

S-06436a Kartlegging og klassifisering av fargesynssvakheter hos skolebarn i alderen 6 til 13 år i Telemarks kommunene Seljord, Bo, og Notodden [2.2006.3415]

S-05388 Kartlegging og klassifisering av fargesynssvakheter hos skolebarn i alderen 6 til 13 år i Kongsberg og Tonsberg kommune

Vi viser til e-post av 12.5.09 med vedlagt tilbakemelding på komiteens merknader og revidert innformasjonsskriv med samtykkeerklæring vedlagt.

Komiteen har ingen merknader til revidert informasjonsskriv med samtykkeerklæring.

Komiteen godkjenner at prosjektet videreføres med de endringer som er beskrevet i skjema for protokolltillegg og endringer og i tilbakemelding på komiteens merknader.

Med vennlig hilsen

Kristian Hagestad (sign.)
Fylkeslege cand.med., spes. i samf.med
Leder

Jørgen Hardang
Sekretær

Letter of reply from Data Inspectorate

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Vår dato: 21.04.2009 Vår ref: 21500 / 2 / JE Deres dato: Deres ref:

TILRÅDING AV BEHANDLING AV PERSONOPPLYSNINGER

Vi viser til melding om behandling av personopplysninger, mottatt 04.03.2009. Meldingen gjelder prosjektet:

21500	*Kartlegging av kvinnelige bærere av fargesynssvakheter i alderen 7-65 år i Kongsberg, Notodden og Bø*
Behandlingsansvarlig	*Høgskolen i Buskerud, ved institusjonens øverste leder*
Daglig ansvarlig	*Rigmor C. Baraas*
Student	*Elise Wiken Dees*

Personvernombudet har vurdert prosjektet, og finner at behandlingen av personopplysninger vil være regulert av § 7-27 i personopplysningsforskriften. Personvernombudet tilrår at prosjektet gjennomføres.

Personvernombudets tilråding forutsetter at prosjektet gjennomføres i tråd med opplysningene gitt i meldeskjemaet, korrespondanse med ombudet, eventuelle kommentarer samt personopplysningsloven/-helseregisterloven med forskrifter. Behandlingen av personopplysninger kan settes i gang.

Det gjøres oppmerksom på at det skal gis ny melding dersom behandlingen endres i forhold til de opplysninger som ligger til grunn for personvernombudets vurdering. Endringsmeldinger gis via et eget skjema, http://www.nsd.uib.no/personvern/forsk_stud/skjema.html. Det skal også gis melding etter tre år dersom prosjektet fortsatt pågår. Meldinger skal skje skriftlig til ombudet.

Personvernombudet har lagt ut opplysninger om prosjektet i en offentlig database, http://www.nsd.uib.no/personvern/prosjektoversikt.jsp.

Personvernombudet vil ved prosjektets avslutning, 31.12.2014, rette en henvendelse angående status for behandlingen av personopplysninger.

Vennlig hilsen

Vigdis Namtvedt Kvalheim

Janne Sigbjørnsen Eie

Kontaktperson: Janne Sigbjørnsen Eie tlf: 55 58 31 52
Vedlegg: Prosjektvurdering
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Appendix B

Research protocol

Kartlegging av kvinnelige bærere av fargesynssvakheter blant barn i alderen 7-13 år og voksne over 18 år i Kongsberg, Notodden og Bø

Elise Wiken Dees
Høgskolen i Buskerud
Avdeling for optometri og synsvitenskap
23. januar 2009

Veileder: Rigmor C. Baraas

Introduksjon

Alle farger kan "matches" ved hjelp av tre parametere: enten de tre additive primærfargene fiolett, grønn og rød, eller ved å blande de tre subtraktive primærfargene cyan, magenta og gul (Sharpe et al., 1999). Rundt år 1800 fremsatte Thomas Young hypotesen om at trikromatisk fargesyn er et resultat av at mennesket har tre ulike lyssensitive mekanismer (Nathans et al., 1986). I dag vet vi at disse mekanismene er tre ulike fotoreseptorceller (tapper) i menneskets retina. Hver tapp inneholder ulike, spesifikke visuelle pigmenter med forskjellig spektral sensitivitet (Nathans et al., 1986, Neitz and Neitz, 2000).

Fargesyn er evnen til å diskriminere lysets bølgelengder, og de tre tappene har maksimal følsomhet for lys ved ulike bølgelengder; henholdsvis 426, 530 og 557 nm (Merbs and Nathans, 1992, Neitz and Neitz, 2000). Derav navnene short- (S-tapp), medium- (M-tapp) og long wavelength sensitive (L-tapp). Dersom alle tre tappene er til stede foreligger det normalt fargesyn, trikromatisk syn. Evnen til å diskriminere farger avhenger av størrelsen på forskjellene mellom de ulike spektrale sensitivitetene. Altså: Jo større differanse det er mellom maksimalverdien av spektral følsomhet for de ulike tappene, jo bedre vil evnen til å diskriminere farger være (innenfor visse begrensninger) (Asenjo et al., 1994, Neitz and Neitz, 2000). I tillegg til svart, hvit og gråtoner, kan en med normalt fargesyn skille mer enn 100 farger (Neitz and Neitz, 2000).

I tillegg til trikromatisk fargesyn foreligger det også personer som matcher farger ved hjelp av tre primærfarger under uvanlig proporsjoner (anomal trikromat), og noen som kun kan bruke to primærfarger (dikromat). Anomale trikromater har, som normale trikromater, tre typer fotoreseptorer, men den ene inneholder et fotopigment med anomal spektral sensitivitet (Nathans et al., 1986). Anomale trikromater deles i to grupper: Protanomale trikromater mangler L-pigmentet fullstendig, og har to M- (eller M-like) pigment, som normalt differensierer seg ved et lite skifte i maksimal spektral følsomhet, i tillegg til S-pigmentet. Hos deuteranomale trikromater foreligger det to typer L-pigment i tillegg til S-pigmentet. Deuteranomali er den vanligste formen for fargesynssvakhet, både for menn (1/20) og kvinner (3/1000) (Neitz and Neitz, 2000). Insidensen hos menn med deuteranomali (4,63 %) er fire ganger hyppigere enn insidensen for protanomali (1,08 %). For kvinner er insidensen av deuteranomali 0,36 % og protanomali 0,03 % (Sharpe et al., 1999).

De som kun kan bruke to primærfarger til å matche alle farger kalles dikromater, og har kun to av de tre typene fotoreseptorer (Nathans et al., 1986). Dikromate svakheter er den alvorligste av de vanligste, arvede rød-grønne fargesynssvakhetene. Dikromate personer mangler genene som koder for et av pigmentene, og har enten S- og M-pigment (protanop), S- og L-pigment (deuteranop) eller M- og L-pigment (tritanop). Personer med denne typen fargesynssvakhet skiller kun mellom to farger, i tillegg til svart, hvit og grå (Neitz and Neitz, 2000). 1,01 % av menn er protanope, mens hos kvinner er insidensen kun 0,02 %. 1,27 % av menn og kun 0,01 % av kvinnene er deuteranope (Sharpe et al., 1999). Tritanopi er en progressiv tilstand som manifesterer seg ved at personer med samme mutasjoner har ulike grader av fargesynssvakheter. Denne typen fargesynssvakhet er assosiert med en progressiv s-tappdystrofi, og en forstyrrelse i tappmosaikkens regulære mønster. Eldre personer med tritandefekt gjør flere feil på fargesynstester enn det yngre personer med tritandefekter gjør (Baraas et al., 2007). Insidensen av tritanopi er mellom 1:13 000 til 1:65 000 i Storbritannia (Sharpe et al., 1999).

Dersom det foreligger en fargesynssvakhet, vil det være en omorganisering av genene for fotopigment. Genene som koder for L- og M-pigmentene ligger på X-kromosomet. En fargesynssvakhet som skyldes mutasjon på L- eller M-genet, er recessivt nedarvet på X-kromosomet. Dette forklarer den store forskjellen i andel fargesynssvake hos menn og kvinner. Tritansvakheter er autosomal dominant nedarvet, hvor feilen i mutasjonen av S-tapp pigmentet ligger på kromosom 7. Denne fargesynssvakheten får derved en mer lik fordeling mellom kjønn (Neitz and Neitz, 2000).

Individer med to ulike varianter av et gen, for eksempel et recessivt og et dominant gen, kalles heterozygote. Heterozygote bærere av rød-grønne fargesynssvakheter knyttet til X-kromosomet forventes å ha normalt trikromatisk fargesyn (Feig and Ropers, 1978). Dette stemmer imidlertid ikke alltid, da disse ofte viser svake til moderate fargesynssvakheter, og oftere feiler og gjør *flere* feil på Ishihara enn normale trikromater (Feig and Ropers, 1978, Waaler, 1927, Crone, 1959, Jordan and Mollon, 1993, Waaler, 1967). Hos kvinnelige bærere av arvelige fargesynssvakheter vil retina inneholde både normale tapper og tapper med anormal spektral sensitivitet, og evnen deres til å diskriminere farger vil variere fra punkt til punkt på retina (Born et al., 1976, Jordan and Mollon, 1993, Sharpe et al., 1999). Heterozygote har også et større matchingsområde ved bruk av Nagels anomaloskop enn normale trikromater har. Derimot er det ikke avdekket noe systematiske endringer i Rayleigh match midtpunkter, og heller ikke økt antall feilscoringer på Farnsworth Munsell 100-hue test (Jordan and Mollon, 1993). Det har vist seg at bærere av deutansvakheter har den dårligste fargediskrimineringen sammenlignet med normale trikromater og bærere av protandefekter (Hood et al., 2006). Rundt 47 % av den kvinnelige befolkningen er heterozygote (Winderickx et al., 1992) og rundt 15 % av kvinnene er heterozygote bærere av rød-grønn fargesynssvakheter knyttet til X-kromosomet (Jordan and Mollon, 1993), hvorav 4,5 % er bærere av enten protanopia eller deuteranopia, og rundt 11 % er bærere av anomal trikromasi (Sharpe et al., 1999). Bærere av protangenet har redusert lyssensitivitet til langbølget lys. Dette ble først rapportert av Schmidt på 1930-tallet, og kalles derfor for Schmidt's tegn. Schmidt's tegn antas å være et resultat av mosaikkmønsteret i tappene hos bærere av protangenet (Harris and Cole, 2005).

Det foreligger polymorfisk variasjon i aminosyren som kodes på kodon 180, og heterozygote kvinner forventes derfor å ha retinale områder med enten SER eller ALA på kodon 180 på L-pigmentet. Denne X-knyttede polymorfismen skyldes trolig X-inaktivering hos kvinner, og skaper et skifte i den spektrale sensitiviteten mellom to pigmenter. Dette fører til store variasjoner i rød-grønn fargediskriminering (Winderickx et al., 1992, Merbs and Nathans, 1992).

Barn, både de med normalt trikromatisk fargesyn og de som er fargesvake, gjør flere feil på fargesynstester, og jo eldre de blir, desto færre falske positive svar foreligger. Dette har blitt vist med flere fargesynstester, blant annet Ishihara og HRR (Hill et al., 1982).

Bakgrunn

Det ble i 2006-07 utført et fargesynsstudium hvor 1445 gutter og 1518 jenter i alderen 6-13 år deltok. Barna var elever ved barneskoler i Kongsberg, Notodden, Bø og Tønsberg. Dersom Tønsberg utelukkes, var det 937 gutter og 959 jenter som deltok i studien. Deltakerne ble først testet med The Neitz Test of Color Vision (NTCV) (Neitz and Neitz, 2001). Alle som gjorde en eller flere feil på denne klasseromstesten ble retestet med NTCV og fjerde utgave av Hardy-Rand-Rittler-test (HRR) (Bailey et al., 2004, Cole et al., 2006). Kriteriet for å bli klassifisert som fargesynssvak var en eller flere feil på NTCV, og to eller flere feil på HRR (Cole et al., 2006). Ved å bruke dette kriteriet, ble 117 gutter (8,09 %) og 45 jenter (2,96 %) klassifisert til å han en rød-grønn fargesynssvakhet. Dersom Tønsberg utelukkes, ble det i Kongsberg, Notodden og Bø funnet at 8,43 % av guttene (n=79) og 2,82 % av jentene (n=27) har en rød-grønn fargesynssvakhet etter ovennevnte kriterium. Dersom en ser kun på resultatene fra Kongsberg, ble 37 gutter klassifisert som fargesvake. Sammenlignet med tidligere studier ble det i denne studien funnet en høyere prosentandel av jentene som ble klassifisert som fargesynssvake. Dette gjelder både når en ser på alle fire kommunene samlet, men også når Tønsberg utelukkes. Da dette er resultater fra screeningstester, kan det ikke med sikkerhet sies at barna faktisk har en fargesynssvakhet før de har blitt testet videre med andre tester (Baraas, 2008).

Problemstilling og formål

Hovedmål

Denne studien har som mål å beskrive forekomsten av kvinnelige bærere som gjør feil på ulike fargesynstester.

Delmål

Ved hjelp av et spørreskjema skal det kartlegges om det foreligger kjente fargesynssvakheter i familien til de 959 jentene fra fargesynstestingen i Kongsberg, Notodden og Bø i 2006-07. På denne måten kan bærer blant disse jentene plukkes ut (jenter med fargesvak far). Dersom det foreligger fargesvake familiemedlemmer, skal det kartlegges hvilke fargesynssvakheter de har. Familiemedlemmene som skal kartlegges vil fortrinnsvis være fedrene til disse jentene. Fargesynet til de 37 guttene som ble klassifisert som fargesvake i Kongsberg i 2006, skal også kartlegges.

Det skal kartlegges hva slags type feil bærerne gjør, hvilke(n) type(r) fargesynssvakhet(er) de er bærere av og om de er hetero- eller homozygote bærere. Bærerne i denne studien vil være jenter og optometristudenter med fargesvake fedre og mødre til de fargesvake guttene.

Ved at ulike aldersgrupper testes, skal det også undersøkes om det foreligger en alderseffekt hos kvinnelige bærere av en fargesynssvakhet. Det vil si: gjør en bærer av en fargesynssvakhet flere feil på tester når de er yngre i forhold til når de er eldre.

Studien vil også kartlegge fargesynet til de 27 jentene som antas å være fargesvake etter fargesynstestingen i perioden 2006-07. Det skal undersøkes om de har en fargesynssvakhet, eller om de er bærere av en fargesynssvakhet. Ved hjelp av NTCV og HRR skal jentene testes for å se om det har skjedd en endring i fargesynet siden forrige gang de ble testet (i perioden 2006-07), også dette for å måle en eventuell alderseffekt.

Design

Denne studien har en deskriptiv design.

Utvalg

Rekruttering

Forsøkspersonene i studien vil bli rekruttert blant barn som deltok i fargesynsstudien utført i Kongsberg, Notodden og Bø i perioden 2006-07, kvinnelige studenter på optometrilinjen på Høgskolen i Buskerud, HiBu, samt barn som har deltatt på skolescreeninger i Kongsberg, utført av Avdeling for optometri og synsvitenskap, AFOS, HiBu, i januar 2008 og 2009. Alle jentene som ble testet i 2006-07 vil motta et spørreskjema som kartlegger fargesynssvakheter i familien. Dersom far er kjent fargesvak, vil disse familiene få forespørsel om far og datter vil delta i studien. Alle jentene som ble klassifisert som mulig fargesvake i studien i 2006-07, vil også bli forespurt om å delta, uansett om far er fargesvak eller ikke. Fargesvake gutter fra testingen i Kongsberg 2006, og AFOS sin skolescreening 2008-09, samt deres mødre, vil bli forespurt om å delta i studien. Alle kvinnelige optometristudenter på HiBu vil også få forespørsel om å delta. Rekrutteringen vil skje ved at informert samtykke (vedlegg nr. 1) sendes hver enkelt familie. Informasjonen vil omfatte studiens formål, utførelse og etiske aspekter.

Utvalg

Utvalget kan deles inn i fire grupper:

1) Under fargesynstestingen i Kongsberg, Notodden og Bø i perioden 2006-07 ble 959 jenter testet. Av disse ble 932 klassifisert som normale trikromater. Disse 932 jentene vil motta et spørreskjema som kartlegger fargesynssvakheter i familien. Jentene som har en fargesvak far vil bli forespurt om å delta i studien (estimert antall fargesvake fedre er 75). Far vil også få forespørsel om å delta i kommende studie.
2) Under fargesynstestingen i 2006-07, ble 27 jenter klassifisert som mulig fargesvake. Disse jentene vil også få forespørsel om å delta, og mottar samme spørreskjema som personene i punkt 1. Dersom jentene har en fargesvak far eller bror, morfar, onkel eller fetter, vil henholdsvis far eller mor også bli forespurt om å delta.
3) Guttene som ble klassifisert som fargesvake under testingen i Kongsberg (n=37), samt deres mødre, vil bli forespurt om å delta i studien. Gutter som blir klassifisert til å ha en

fargesynssvakhet under skolescreening utført av AFOS, HiBu, i januar 2008-09, (n=20), samt deres mødre, vil også inkluderes i studien.

4) Kvinnelige studenter, uansett om far er kjent fargesvak eller ikke, i 1. (n=49) og 3. klasse (n=43) på optometristudiet ved HiBu vil også bli forespurt om delta i studien. Disse jentene vil også motta et spørreskjema for å kartlegge fargesynssvakheter i familien.

Utvalgets størrelse

Utvalgets størrelse vil være på 410 forsøkspersoner.

Inklusjonskriterier

Deltakerne vil være barn i alderen 7-13 år og voksne over 18 år, med normalt eller svekket fargesyn og må tilhøre en av utvalgets fire grupper for å bli inkludert i kommende studie. Alle deltakerne vil være normalt friske, uten okulære eller systemiske sykdommer med innvirkning på øyet (fortrinnsvis fargesyn). Alle må ha skrevet under på og levert en samtykkeerklæring for å kunne delta.

Eksklusjonskriterier

Personer som er blinde eller som har en fysisk og/eller psykisk begrensing som forhindrer de i å utføre testene vil bli ekskludert fra studien. De som ikke har skrevet under på og levert en samtykkeerklæring vil også bli ekskludert fra å delta. Også personer med okulære eller systemiske sykdommer som kan ha innvirkning på øyet vil bli ekskludert fra studien.

Variabler

Variabler for fargesyn

Variabel	Definisjon	Type variabel	Forklaring	Type definisjon
Kjønn	Gutt Jente	Nominell	Påvirkningsvariabel	1. G 2. J
Etnisitet	Kaukasisk Annen	Nominell	Kaukasisk: Europeisk populasjon	1. K 2. A
Type fargesyn	Normal trikromat Protan Deutan Tritan Monokromat Bærer	Nominell	Utfallsvariabel	1. NT 2. P 3. D 4. T 5. M 6. B
Grad ved NTCV	Behavior 1 Behavior 2 Behavior 3 Tritan behavior 1 Tritan behavior 2	Ordinell	Svak Moderat Sterk Moderat Sterk	1. B1 2. B2 3. B3 4. TB1 5. TB2
Grad ved HRR	Rød-grønn 1 Rød-grønn 2 Rød-grønn 3 Tritan 1 Tritan 2	Ordinell	Svak Moderat Sterk Moderat Sterk	1. RG1 2. RG2 3. RG3 4. T1 5. T2
Grad Ishihara	Deutan 1 Deutan 2 Protan 1 Protan 2	Ordinell	Moderat Sterk Moderat Sterk	1. D1 2. D2 3. P1 4. P2
Grad anomaloskop	Normal trikromat Protanomali Sterk protanomali Protanop Deuteranomali Sterk deuteranomali Deuteranop Tritanop Akromatopsi Diagnosis not possible	Nominell	 Anomal trikromat Dikromat Anomal trikromat Dikromat	1. N 2. PA 3. EPA 4. P 5. DA 6. EDA 7. D 8. T 9. A 10. DNP
Grad FM 100 Hue	Total error scores Total partial error scores, red-green	Nominell	 Caps: 13-33, 55-75	1. TES 2. R-G

	Total partial error scores, blue-yellow		Caps: 1-12, 34-54, 76-85	3. B-Y
Grad Medmont C-100	Normal trikromat Deureranomali Deuteranop Protanomali Protanop	Nominell		1. N 2. DA 3. D 4. PA 5. P
Grad CTT	Normal trikromat Protanomali Sterk protanomali Protanop Deuteranomali Sterk deuteranomali Deuteranop Tritanop Not available	Nominell	 Anomal trikromat Dikromat Anomal trikromat Dikromat Missing data	1. N 2. PA 3. EPA 4. P 5. DA 6. EDA 7. D 8. T 9. NA

Variabler for spørreskjema

Variabel	Definisjon	Type variabel	Forklaring	Type definisjon
Id. nr.				1,2,3... osv
Fødselsår		Intervall		1995, 1996...etc.
Testet fargesyn før studien i 2006-07		Nominell	Mange med fargesynssvakheter har aldri testet fargesynet	1. Ja 2. Nei 3. Vet ikke
Visshet om eventuell fargesynssvakhet		Nominell	Mange er ikke klar over at de er fargesvake	1. Ja 2. Nei 3. Vet ikke
Problemer med å skille ulike farger		Nominell	Fargekoding kan skape problemer hos fargesvake personer	1. Ja 2. Nei 3. Vet ikke
Familiemedlemmer med fargesynssvakhet		Nominell	Kartlegging av bærere	1. Ja 2. Nei 3. Vet ikke

Datainnsamling

Datainnsamlingen vil forgå ved hjelp av fargesynstestene NTCV, HRR, anomaloskopet (Rayleigh og Moreland match), Ishihara, Medmont C-100, CCT og FM Hue, samt et spørreskjema (vedlegg nr. 2) som vil bli sendt ut i forkant av studien. Spørreskjemaet vil kartlegge hvem som skal inkluderes i studien. Alle deltakerne skal testes med NTCV, HRR, Ishihara, Medmont C-100 og FM 100 Hue for å se om bærere gjør feil på de ulike fargesynstestene. Deltakere over 18 år skal i tillegg testes med anomaloskopet (Rayleigh og Moreland match). De 27 jentene som ble klassifisert som fargesvake under fargesynstestingen i perioden 2006-2007, skal også testes for å se om det er en endring av resultatet siden forrige gang de ble testet og om de er bærere eller om de faktisk har en fargesynssvakhet. Jentene fra optometrilinjen skal i tillegg til de andre testene også testes med CCT. Fedrene og sønnene i denne studien skal testes for å kartlegge, klassifisere og gradere fargesynssvakheten de har. Forventet tidsforbruk per test vil være: NTCV og HRR, 30 min; Ishihara, 5 min; FM 100 Hue, 15 min; Medmont C-100, 5 min; CCT, 30 min og anomaloskopet 60 min. Dette innebærer at det beregnes ca 1 time med testing per forsøksdeltaker under 18 år; over 18 år, 2 timer og optometristudentene, 2,5 timer. Deltakerne fra Kongsberg skal testes på forskningslaboratorium for fargesyn på HiBu, de andre deltakerne testes på barneskoler i Notodden og Bø. Alle fargesynstestene blir utført under kontrollerte lysforhold.

Spørreskjemaet vil kartlegge om far har en fargesynssvakhet, og om det foreligger fargesynssvakheter hos andre familiemedlemmer. Svarene vil være med på å avgjøre hvem som skal bli testet videre, og hvor stort det totale utvalget blir. Spørreskjemaet vil inneholde en forside med forsøkspersonens kontaktinformasjon, slik at det lar seg gjøre å avtale tid for utføring av testene ved jentenes respektive skoler. Etter endt testing vil dette arket fjernes og makuleres, spørreskjemaet vil kun være identifisert med et anonymt identifikasjonsnummer.

Fargesynstester som inngår i studien

Richmond Products Hardy-Rand-Rittler 2002 (HRR) er en pseudoisokromatisk platetest og kan avdekke, skille og gradere både tritan, protan og deutan fargesynssvakheter (Cole et al., 2006, Bailey et al., 2004). Dersom testpersonen gjør to feil, vil han/hun *sannsynligvis* ha en fargesynssvakhet. Med et slikt kriterium vil det være en risiko (5:200) for at personen blir misdiagnostisert til å ha en fargesynssvakhet. Testens sensitivitet og spesifisitet vil da være henholdsvis 0,98 og 1,0 (Cole et al., 2006).

The Neitz Test of Color Vision (NTCV) er en klasseromstest hvor testpersonen skal identifisere ulike symboler. Testen er spesielt utviklet for barn i godt belyste klasserom med fluoriserende lysstoffrør kombinert med dagslys, og avdekker og klassifiserer en eventuell fargesynssvakhet (Neitz and Neitz, 2001, Neitz et al., 2001). Som HRR avdekker også NTCV både deutan, protan og tritandefekter (Neitz and Neitz, 2001, Bailey et al., 2004, Cole et al., 2006). Alle som gjør en eller flere feil på NTCV, vil retestes med et annet ark fra samme test. Dersom testpersonen også feiler på retesten, vil han/hun klassifiseres som fargesvak (Neitz et al., 2001).

Ishihara ble først publisert i 1906 og er trolig den mest brukte fargesynstesten internasjonalt. Testen betegnes fortsatt som gullstandarden for rask screening av fargesynssvakheter (Dain, 2004). Både HRR og NTCV avdekker tritandefekter, hvilket Ishihara *ikke* gjør. HRR antas derfor å være en bedre test for å avdekke fargesynssvakheter enn Ishihara (Cole et al., 2006). Nærmere halvparten av personer med normalt fargesyn gjør feil på Ishihara-testen (Neitz and Neitz, 2000). Testen utført i sin helhet er veldig nær 1,0 i både sensitivitet og spesifisitet (Dain, 2004).

HRR, NTCV og Ishihara benyttes som screeningstester. Det vil si, dersom testpersonen feiler på en av disse testene, er han/hun trolig fargesvak. Testpersonen vil derfor testes med flere tester for å kartlegge og klassifisere en eventuell fargesynssvakhet.

Farnsworth Munsell 100 Hue-test (FM 100 Hue) er en diskriminerings- og sorteringstest utviklet av Farnsworth tidlig på 1940-tallet. Testen er basert på like persepsjonelle steg, hvor alle fargene har samme metning og lyshet, og varierer derfor kun i fargetone. Fem farger (rød, gul, grønn, blå og purpur) benyttes for å lage de ulike fargene på testens 85 brikker. Testpersonen skal sortere brikkene, og resultatet av testen plottes inn i et diagram. Det dannes så en figur av feilene karakterisert av svakheten de har, enten det er protan-, deutan- eller tritandefekt (Dain, 2004, Kinnear and Sahraie, 2002).

For å oppnå riktig belysning, vil HRR, Ishihara og FM 100 utføres under en spesiell lampe, True Daylight Illuminator, belysning som tilsvarer dagslys.

Anomaloskopet (Rayleigh og Moreland match) tester ved hjelp av additive fargeblander fargesynet og dets eventuelle anomaliteter og defekter. Ved Rayleigh match blander testpersonen et bestemt spektrum rødt og et bestemt spektrum grønt, slik at det i bestemte forhold oppstår en fargeoppfattelse som er lik den som oppstår når øyet stimuleres med en viss monokromatisk spektrum gul: Rød + Grønn = Gul. Hver testperson vil ha en unik Rayleigh match, karakterisert av fargeblandingen og lyshetsgraden. Ved hjelp av dette kan en persons eventuelle fargesynssvakhet klassifiseres og graderes (Linksz, 1964). En Rayleigh match vil skile anomale trikromater fra normale trikromater, og dikromater fra anormale trikromater (Dain, 2004). Tritandefekter kan kartlegges ved Moreland match, hvor: Blå + Grønn = Cyan + gul (Oculus, 1999). Anomaloskopet betegnes gjerne som en diagnostiserende test.

The Cambridge Colour Vision Test (CCT) tester pasientens fargekontrast, og kan benyttes til enten en rask screening (trivektortest) av fargesynssvakheter, eller en mer detaljert undersøkelse av en pasients fargediskriminering. Ved hjelp av "staircase"-prosedyre blir den kromatiske sensitiviteten målt langs ulike fargeakser. CCT sitt lengste testprogram tester

hele diskrimineringsellipsen, slik at et eventuelt sensitivitetstap vil synliggjøres som en ellipse rundt aksen til feilingsområdet i et CIE-diagram (Mollon and Regan, 2000, Regan et al., 1994).

Medmont C-100 test (C-100) måler relativ spektral sensitivitet for rødt og grønt lys ved hjelp av flimmerfotometri. Den presenterer rødt og grønt lys emittert fra to alternerende LED lysdioder. Pasienten justerer den relative intensiteten til det oppstår ingen eller minimum flimmer. C-100 skiller protan- fra deutandefekter, og avdekker om pasienten er bærer eller faktisk har en fargesynssvakhet. Den avdekker også Schmidt's tegn, da disse pasientene vil ha redusert lyssensitivitet til rødt lys (Harris and Cole, 2005).

Analyse

Rådataene foreligger i papirformat, i form av skjemaer utfylt under testing. Alle data vil bli manuelt overført til Microsoft Office Excel 2003. Forsøkspersonenes navn vil ikke bli overført, kun identifikasjonsnummer. Alle data vil bli kontrollert med hensyn til avvik. Urealistiske verdier vil bli kontrollert opp mot rådataene. Dersom verdiene fortsatt anses som urealistiske, vil de bli ekskludert og behandlet som forsvunne data. Rådataene vil bli oppbevart på en tape, og det vil jevnlig bli tatt sikkerhetskopi av analysematerialet og avhandlingen.

Dataene vil bli registrert, behandlet og analysert fortløpende etter hvert som testingen utføres. Analysene vil vise om bærere av fargesynssvakheter gjør feil på fargesynstestene, hvilken fargesynssvakhet de er bærere av, og hvor mange av mange av jentene som har en fargesynssvakhet, samt type og grad. Analysene vil også gi hvem og hvor mange i jentenes familie som har en fargesynssvakhet, samt hvilken fargesynssvakhet de har. Resultatene vil bli sammenholdt med studien utført i Kongsberg, Notodden og Bø i 2006-2007.

All statistisk analyse vil bli utført i SPSS versjon 15,0 for Windows. Statistisk signifikansnivå settes til $p < 0,05$. Det antas at utvalget ikke vil være normalfordelt.

Prosjektorganisering

Student:	Elise Wiken Dees
Veileder:	Rigmor C. Baraas
Medarbeider :	Rigmor C. Baraas, Lene A. Hagen
Analyse og publisering:	Elise Wiken Dees

- Student har ansvar for gjennomføring av prosjektet. Dette innebærer planlegging og uføring av prosjektet, overholde tidsplan, innsamling, behandling og analyse av data, økonomi, utførelse av avhandling, evaluering av prosjektet og publisering av materialet.
- Veileder skal veilede prosjektleder og gi faglig og praktisk hjelp. Hun skal også kontrollere at det er fremgang i arbeidet.
- Medarbeider har ansvar for å hjelpe til med innsamling av data i Notodden og Bø.

Personell, utstyr, ressurser

Personell

Alt personell er autoriserte optikere.
Estimert antall timer per medarbeider (ved hundre prosent oppmøte): 44 timer
Estimert antall timer student (ved hundre prosent oppmøte): 619 timer

Utstyr

Til datainnsamlingen vil følgende utstyr, som er tilgjengelig ved AFOS, benyttes
- NTCV, HRR-testen, Anomaloskop, Ishihara, FM 100 Hue, Medmont C-100 test og CCT
- Lysboks med transformator

Annet utstyr som vil bli benyttet i forbindelse med analyse/utarbeidelse av avhandling:
- PC med Word, Excel, PowerPoint og SPSS

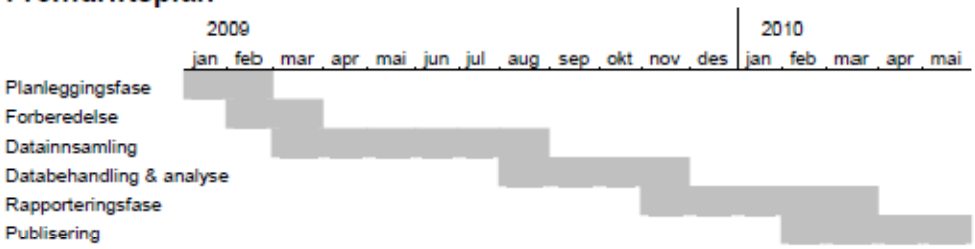
- Kontorrekvisita, kopimaskin og printer

Kostnader og finansieringsplan

Finansieringsplan

Studien er finansiert gjennom forskningsmidler fra AFOS, HiBu.

Fremdriftsplan



Publisering

Masteroppgaven skal resultere i en rapport. Det skal også publiseres en artikkel i et fagfellevurdert blad. Resultatene skal dessuten presenteres ved hjelp av en poster og/eller et foredrag på en internasjonal og en nasjonal konferanse. Prosjektleder vil stå som forfatter på den ovennevnte publiseringen.

Etikk

Det er ingen risiko forbundet med testene som skal uføres i denne studien, heller ikke spesielle ubehag. Det er mange tester som skal gjennomføres, og forsøkspersonene kan bli slitne og umotiverte siden testingen vil ta noe tid (estimert tid per deltaker er fra 1 til 2,5 timer). Spesielt kan for eksempel testing med anomaloskopet virke slitsom og vanskelig. Det er derfor viktig at forsøkspersonene får tilstrekkelig med forklaring av prosjektets formål og utførelse i forkant av studien, og hvordan de ulike testene fungerer før de blir utført. De skal også bli oppfordret til å stille spørsmål både i forkant og underveis i testingen. Ved behov vil det bli lagt til rette for pauser mellom de ulike testene. Dersom det under testing kommer frem at noen av studiedeltakerne vil ha behov for, eller at det vil være fordelaktig for dem, å ta en fullstendig og eventuelt utvidet synsundersøkelse, vil de bli oppfordret til enten å ta kontakt med HiBu v/AFOS, eller sin lokale optiker.

Det er utarbeidet et informert samtykkeskjema (se vedlegg nr. 1) som forsøkspersonene må undertegne i forkant av studien. For barn under 12 år er det foreldre/foresatte som gir samtykke om deltakelse i studien, men barnets standpunkt bør vektlegges i avgjørelsen. Barn som er 12 år eller eldre må i tillegg til foreldre/foresattes samtykke gi *sitt* samtykke til å delta i studien. Forsøkspersonene kan avstå fra å delta, og kan dersom de ønsker det når som helst trekke sitt samtykke og derved gå ut av studien, uten å måtte oppgi noen grunn og uten negative konsekvenser for personen.

Alle personlige data vil behandles konfidensielt. Forsøkspersonene vil få et unikt identifikasjonsnummer som registreres i studiens database. Dette id-nummeret vil bli brukt i analysen, og sikrer anonymitet og at sensitive personopplysninger blir korrekt ivaretatt. Analysedataene vil ikke inneholde noen personopplysninger. Listen som knytter forsøksperson og id-nummer sammen vil bli oppbevart på en sikker måte hos prosjektleder, slik at navn ikke kan knyttes til id-nummer dersom dataene skulle komme på avveie. Skjemaene som blir brukt i forbindelse med testene vil systematiseres og oppbevares i mapper merket med den enkelte forsøkspersons id-nummer, innelåst i et brannsikkert skap.

For å få gjennomført prosjektet skal det søkes om godkjenning fra Regional etisk komité (REK). Prosjektet skal også meldes til personvernombudet, siden det i denne studien

behandles person- og helseopplysninger. Det vil dessuten være elektronisk behandling av personopplysninger, og også opprettelse av et manuelt personregister med sensitive personopplysninger. Ved meldeskjema skal det vedlegges kopi av spørreskjema, registreringsskjema, informasjonsskriv og samtykkeerklæring. Kopi av godkjenning fra REK skal også legges ved meldeskjemaet når studien meldes til personvernombudet.

Vedlegg

1. Skjema: Informert samtykkeskjema
2. Spørreskjema foreldre/foresatte
3. Spørreskjema kvinnelige optometristudenter

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Appendix C

Agreement with Bø municipality

HØGSKOLEN
i Buskerud

Vår ref: 2007/249 Saksbeh: RCB

Avtale om skolescreening mellom
Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap
og Bø Kommune

Det inngås avtale om å utføre fargesynstesting på skolebarn i alderen 9-13 år for perioden 01.10.09 – 31.05.10. Dette er skolebarn som tidligere har deltatt i en fargesynsscreening som ble utført våren 2007.

Student Elise Wiken Dees ved Mastergradsstudie i synsvitenskap ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap, skal i løpet av skoleåret 2009/10 utføre et forskningsprosjekt som en del av hennes mastergrad. Formålet med prosjektet er å kartlegge forekomsten av kvinnelige bærere av rød-grønne fargesynssvakheter som gjør feil på ulike fargesynstester. Alle kvinner som har en far eller en sønn med en rød-grønn fargesvakhet er bærere. Studien skal også vurdere betydningen av hva slags type feil bærere gjør på de ulike testene i forhold til hvilken fargesynssvakhet de er bærere av, og hvor gamle de er. Derfor skal det også kartlegges hvilke fargesynssvakheter som foreligger i familien til testpersonene, det vil si, fedrene til jentene og sønnene til mødrene i studien. Prosjektet skal teste jenter i alderen 9-13 år som deltok på fargesynsscreeningen våren 2007 i Bø (se vedlagt informasjonsfolder med samtykkeerklæring). 1.amanuensis Rigmor C Baraas har veiledningsansvar for Elise Wiken Dees.

Foreldre/foresatte blir i informasjonsfolderen gjort oppmerksom på at deltakelse i prosjektet er frivillig, og uten noen form for risiko. Deltakerne kan når som helst trekke seg fra prosjektet uten å oppgi grunn. Prosjektet er godkjent av Regional komité for medisinsk forskningsetikk, Sør-Øst (se vedlagt kopi av brev).

På grunn av taushetsplikt, vil ikke lærer eller medelever bli gjort oppmerksom på hvilke elever som har en fargesvakhet. Elevene vil ikke få vite resultatet av testen samme dag, men de som ønsker kan senere få tilsendt et informasjonsbrev.

Det foreligger ikke vederlag for partene tilknyttet denne avtalen.
Studentens utgifter til materiell og reiser blir dekket av prosjektmidler.

Bø/Kongsberg 25.09.09

Helge Vreim
Kommunalsjef
Bø Kommune

Janne Dugstad
Dekan, AFOS, HiBu

Agreement with Notodden municipality

HØGSKOLEN
i Buskerud

Vår ref: 2007/249 Saksbeh: RCB

Avtale om skolescreening mellom
Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap
og Notodden Kommune

Det inngås avtale om å utføre fargesynstesting på skolebarn i alderen 9-13 år for perioden 01.10.09 – 31.05.10. Dette er skolebarn som tidligere har deltatt i en fargesynsscreening som ble utført våren 2007.

Student Elise Wiken Dees ved Mastergradsstudie i synsvitenskap ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap, skal i løpet av skoleåret 2009/10 utføre et forskningsprosjekt som en del av hennes mastergrad. Formålet med prosjektet er å kartlegge forekomsten av kvinnelige bærere av rød-grønne fargesynssvakheter som gjør feil på ulike fargesynstester. Alle kvinner som har en far eller en sønn med en rød-grønn fargesvakhet er bærere. Studien skal også vurdere betydningen av hva slags type feil bærere gjør på de ulike testene i forhold til hvilken fargesynssvakhet de er bærere av, og hvor gamle de er. Derfor skal det også kartlegges hvilke fargesynssvakheter som foreligger i familien til testpersonene, det vil si, fedrene til jentene og sønnene til mødrene i studien. Prosjektet skal teste jenter i alderen 9-13 år som deltok på fargesynsscreeningen våren 2007 i Notodden (se vedlagt informasjonsfolder med samtykkeerklæring). 1.amanuensis Rigmor C Baraas har veiledningsansvar for Elise Wiken Dees.

Foreldre/foresatte blir i informasjonsfolderen gjort oppmerksom på at deltakelse i prosjektet er frivillig, og uten noen form for risiko. Deltakerne kan når som helst trekke seg fra prosjektet uten å oppgi grunn. Prosjektet er godkjent av Regional komité for medisinsk forskningsetikk, Sør-Øst (se vedlagt kopi av brev).

På grunn av taushetsplikt, vil ikke lærer eller medelever bli gjort oppmerksom på hvilke elever som har en fargesvakhet. Elevene vil ikke få vite resultatet av testen samme dag, men de som ønsker kan senere få tilsendt et informasjonsbrev.

Det foreligger ikke vederlag for partene tilknyttet denne avtalen.
Studentens utgifter til materiell og reiser blir dekket av prosjektmidler.

Bø/Kongsberg 02.09.09

Anne Grete Rønningsdalen
Helse og Sosialsjef
Notodden Kommune

Janne Dugstad
Dekan, AFOS, HiBu

Agreement with Kongsberg municipality

HØGSKOLEN
i Buskerud

Vår ref: 2007/249 Saksbeh: RCB

Avtale om skolescreening mellom
Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap
og Kongsberg Kommune

Det inngås avtale om å utføre fargesynstesting på skolebarn i alderen 9-13 år for perioden 01.10.09 – 31.05.10. Dette er skolebarn som tidligere har deltatt i en fargesynsscreening som ble utført våren 2006.

Student Elise Wiken Dees ved Mastergradsstudie i synsvitenskap ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap, skal i løpet av skoleåret 2009/10 utføre et forskningsprosjekt som en del av hennes mastergrad. Formålet med prosjektet er å kartlegge forekomsten av kvinnelige bærere av rød-grønne fargesynssvakheter som gjør feil på ulike fargesynstester. Alle kvinner som har en far eller en sønn med en rød-grønn fargesvakhet er bærere. Studien skal også vurdere betydningen av hva slags type feil bærere gjør på de ulike testene i forhold til hvilken fargesynssvakhet de er bærere av, og hvor gamle de er. Derfor skal det også kartlegges hvilke fargesynssvakheter som foreligger i familien til testpersonene, det vil si, fedrene til jentene og sønnene til mødrene i studien. Prosjektet skal teste jenter i alderen 9-13 år som deltok på fargesynsscreeningen våren 2006 i Kongsberg (se vedlagt informasjonsfolder med samtykkeerklæring). 1.amanuensis Rigmor C Baraas har veiledningsansvar for Elise Wiken Dees.

Foreldre/foresatte blir i informasjonsfolderen gjort oppmerksom på at deltakelse i prosjektet er frivillig, og uten noen form for risiko. Deltakerne kan når som helst trekke seg fra prosjektet uten å oppgi grunn. Prosjektet er godkjent av Regional komité for medisinsk forskningsetikk, Sør-Øst (se vedlagt kopi av brev).

På grunn av taushetsplikt, vil ikke lærer eller medelever bli gjort oppmerksom på hvilke elever som har en fargesvakhet. Elevene vil ikke få vite resultatet av testen samme dag, men de som ønsker kan senere få tilsendt et informasjonsbrev.

Det foreligger ikke vederlag for partene tilknyttet denne avtalen.
Studentens utgifter til materiell og reiser blir dekket av prosjektmidler.

Kongsberg 15.09.09

Ole Bjørn Herland
Helse- og Sosialsjef
Kongsberg Kommune

Janne Dugstad
Dekan, AFOS, HiBu

Appendix D

Informed written consent

Kartlegging av kvinnelige bærere av fargesynssvakheter

Forespørsel om deltakelse i forskningsprosjektet

"Kartlegging av kvinnelige bærere av fargesynssvakheter blant barn i alderen 7-13 år og voksne over 18 år i Kongsberg, Notodden og Bø"

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie for å kartlegge kvinnelige bærere av fargesynssvakheter og å beskrive forekomsten av kvinnelige bærere som gjør feil på ulike fargesynstester. Det skal kartlegges hva slags type feil bærere gjør på de ulike testene, samt hvilken fargesynssvakhet de er bærere av. Ulike aldersgrupper skal testes i denne studien, slik at det kan undersøkes om det foreligger en alderseffekt hos kvinnelige bærere av en fargesynssvakhet. Det vil si: gjør en bærer av en fargesynssvakhet flere feil på tester når de er yngre i forhold til når de er eldre. Det skal også kartlegges hvilke fargesynssvakheter som foreligger i familien til testpersonene, det vil si, fedrene til jentene og sønnene til mødrene i studien.

Deltakerne vil rekrutteres fra tre ulike grupper, og du er blitt forespurt om å delta fordi du hører til i en av følgende grupper:

Gruppe A Deltakerne i denne gruppen rekrutteres fra fargesynsstudien som ble utført i Kongsberg, Notodden og Bø i perioden 2006-07. Alle jentene som deltok i denne studien vil motta et spørreskjema som kartlegger fargesynssvakheter i familien. Dersom far er fargesvak, vil jenta og faren bli forespurt om å delta i denne studien. Deltakerne vil bli invitert til henholdsvis Høgskolen i Buskerud, en barneskole i Notodden eller en barneskole i Bø for å gjennomføre fargesynstestingen.

Gruppe B Deltakerne fra denne gruppen rekrutteres fra 1. og 3. klasse optometri ved Høgskolen i Buskerud. Alle jentene i disse to klassene vil motta et spørreskjema som kartlegger fargesynssvakheter i familien. De vil også få forespørsel om å delta i kommende studie. Fargesynstestingen for denne gruppen vil bli utført på Høgskolen i Buskerud.

Gruppe C Deltakerne fra denne gruppen rekrutteres fra fargesynsstudien som ble utført i Kongsberg våren 2006, og skolescreeningen utført av Avdeling for optometri og synsvitenskap januar i 2008 og 2009 i Kongsberg kommune. Alle guttene som ble klassifisert som fargesvake, samt deres mødre, vil bli forespurt om å delta i kommende studie. Deltakerne fra denne gruppen vil bli invitert til Høgskolen i Buskerud for å utføre fargesynstestene.

Ansvarlig for studien er 1. amanuensis Rigmor C. Baraas ved Avdeling for Optometri og Synsvitenskap, Høgskolen i Buskerud.

Hva innebærer studien?
Studien er delt i to. Du vil bli bedt om særskilt samtykke for hvert av delstudiene. Ved å samtykke om å delta i delstudium 1 vil du svare på et spørreskjema som kartlegger fargesynssvakheter i familien din. I delstudium 2 vil fargesynet ditt, og eventuelt også familiemedlemmers fargesyn, bli testet. Alle studiedeltakerne vil bli testet med fargesynstestene the Neitz test of color vision (NTCV), HRR, Ishihara, Medmont C-100 og Farnsworth Munsell 100 Hue test. Alle deltakere over 18 år vil i tillegg testes med anomaloskopet (Rayleigh og Moreland match). Deltakerne fra optometriklassene vil også testes med Cambridge Colour Test (CCT).

Mulige fordeler og ulemper
Fordeler ved deltakelse i kommende studie, er at du vil få en grundig undersøkelse av fargesynet ditt. Du vil få klassifisert en eventuell fargesynssvakhet om du har det. Undersøkelsen innebærer bruk av 5 forskjellige fargesynstester som alle studiedeltakerne vil bli testet med, samt at de over 18 vil bli testet med en test i tillegg og deltakerne fra optometriklassene testes med ytterligere en test. Det beregnes en time med testing per forsøksdeltaker under 18 år, over 18 år, 2 timer og optometristudentene, 2,5 timer. Det understrekes at alle tester som blir utført er uten noen form for risiko og intet ubehag, og de blir av de fleste oppfattet som goy å være med på.

Hva skjer med informasjonen om deg?
Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Resultatene fra de ulike fargesynstestene vil benyttes slik som beskrevet i hensikten med studien.

Navn, fødselsår, kjønn, etnisitet og opplysninger om fargesynet ditt vil bli registrert, og som prosjektdeltaker vil du tildeles en kode. I studien vil deltakerne bli identifisert gjennom denne koden. Koden og navneliste vil bli oppbevart separat. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres. Alle opplysninger vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger.

Studien er godkjent av Regional komité for medisinsk forskningsetikk og meldt til Personvernombudet for forskning.

Datamaterialet blir anonymisert etter at studien er gjennomført, senest innen 31.12.2014.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling.

Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte:

Rigmor C. Baraas
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg
Tlf: 32 86 97 87
E-mail: rigmor.baraas@hibu.no

Ytterligere informasjon om studien finnes i kapittel *A* – *utdypende forklaring av hva studien innebærer.*
Ytterligere informasjon om personvern og forsikring finnes i kapittel B – *Personvern, økonomi og forsikring.*

Samtykkeerklæring følger etter kapittel B.

Kapittel A- utdypende forklaring av hva studien innebærer

- Kriterier for deltakelse: Normalt friske personer i alderen 7-13 år og voksne over 18 år, både med normalt eller svekket fargesyn, vil bli rekruttert fra tidligere studie utført i Kongsberg, Notodden og Bo og jenter i 1. og 2. klasse optometri ved HiBu.
- Bakgrunnsinformasjon: Bærere av fargesynssvakheter forventes å ha normalt trikromatisk fargesyn. Dette stemmer imidlertid ikke alltid, da disse ofte viser svake til moderate fargesynssvakheter, og oftere feiler og gjør ***flere*** feil på ulike fargesynstester enn normale trikromater. Rundt 15 % av kvinner er bærere av rod-grønn fargesynssvakhet.
- Tidsskjema: Datainnsamlingen startes opp i februar/mars 2009.
- Fordeler ved deltakelse er at du vil få en grundig undersøkelse av fargesynet ditt. Du vil få klassifisert en eventuell fargesynssvakhet om du har det. Det understrekes at alle tester som blir utført er uten noen form for risiko og intet ubehag, og de blir av de fleste oppfattet som gøy å være med på.
- Det vil ikke bli gitt noen kompensasjon eller dekning av utgifter for deltakere.

Kapittel B - Personvern, økonomi og forsikring

Personvern
Opplysninger som registreres om deg er navn, fodselsår, etnisitet, resultater fra fargesynstestingen samt kontaktinformasjon.

Andre forskere som har tilgang til datamaterialet er medarbeidere på studien: Stipendiat Lene A. Hagen og masterstudent Elise Wiken Dees, begge ansatt ved Avdeling for optometri og synsvitenskap, Høgskolen i Buskerud. Alle som får innsyn har taushetsplikt.

Avdeling for optometri og synsvitenskap, Høgskolen i Buskerud, ved dekan Janne Dugstad er databehandlingsansvarlig.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Økonomi
Studien er finansiert gjennom forskningsmidler fra Avdeling for optometri og synsvitenskap, avdeling Kongsberg, Høgskolen i Buskerud.

Forsikring
Pasientskadeerstatningsordningen.

Informasjon om utfallet av studien
Du har som deltaker rett til å få informasjon om utfallet og resultatet av studien.

Samtykke til deltakelse i delstudie 1, gruppe A

- Jeg er villig til å delta i studien
- Jeg har lest og forstått informasjonen som er gitt
- Jeg er inneforstått at deltakelse er frivillig, og jeg kan trekke meg fra studien når som helst og uten å oppgi noen grunn

Sted Dato

Barnets navn (trykte bokstaver)

Fars navn (trykte bokstaver)

Signatur far, barn fylt 12 år må i tillegg signere selv

Samtykke til deltakelse i delstudie 1, gruppe B

- Jeg er villig til å delta i studien
- Jeg har lest og forstått informasjonen som er gitt
- Jeg er inneforstått at deltakelse er frivillig, og jeg kan trekke meg fra studien når som helst og uten å oppgi noen grunn

Sted Dato

Navn (trykte bokstaver)

Signatur

Samtykke til deltakelse i delstudie 2, gruppe A

- Jeg er villig til å delta i studien
- Jeg har lest og forstått informasjonen som er gitt
- Jeg har hatt mulighet til å stille spørsmål underveis
- Jeg er inneforstått at deltakelse er frivillig, og jeg kan trekke meg fra studien når som helst og uten å oppgi noen grunn

Sted Dato

Barnets navn (trykte bokstaver)

Fars navn (trykte bokstaver)

Signatur far, barn fylt 12 år må i tillegg signere selv

Jeg bekrefter å ha gitt informasjon om studien

(Signatur, rolle i studien) Dato

Samtykke til deltakelse i delstudie 2, gruppe B

- Jeg er villig til å delta i studien
- Jeg har lest og forstått informasjonen som er gitt
- Jeg har hatt mulighet til å stille spørsmål underveis
- Jeg er inneforstått at deltakelse er frivillig, og jeg kan trekke meg fra studien når som helst og uten å oppgi noen grunn

Sted Dato

Navn (trykte bokstaver)

Signatur

Jeg bekrefter å ha gitt informasjon om studien

(Signatur, rolle i studien) Dato

Samtykke til deltakelse i delstudie 2, gruppe C

- Jeg er villig til å delta i studien
- Jeg har lest og forstått informasjonen som er gitt
- Jeg har hatt mulighet til å stille spørsmål underveis
- Jeg er inneforstått at deltakelse er frivillig, og jeg kan trekke meg fra studien når som helst og uten å oppgi noen grunn

Sted Dato

Barnets navn (trykte bokstaver)

Mors navn (trykte bokstaver)

Signatur mor, barn fylt 12 år må i tillegg signere selv

Jeg bekrefter å ha gitt informasjon om studien

(Signatur, rolle i studien) Dato

Appendix E

Questionnaire parents/superiors

Kartlegging av kvinnelige bærere av fargesynssvakheter Spørreskjema

SPØRRESKJEMA TIL FORELDRE/FORESATTE

Fødselsår datter/sønn: _____

- Har deres datter/sønn testet fargesynet sitt før eller etter hun/han deltok på fargesynsscreeningen vinteren 2006/2007?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

- Har deres datter/sønn en kjent fargesynssvakhet (ofte kalt fargeblindhet eller rød-grønn fargeblindhet)?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

- Har deres datter/sønn problemer med å skille noen farger fra hverandre?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

Hvis ja, hvilke farger:

_____

- Har noen i deres datters/sønns nære familie en kjent fargesynssvakhet, og i så fall hvem?

Ja ☐ Nei ☐ Vet ikke ☐

Hvis Ja, vennligst noter nedenfor hvem (far/mor/bror/morfar/onkel/fetter etc.) og om disse familiemedlemmene hører til på mors eller fars side av familien. Dersom kjent, er det fint om dere noterer hvilken fargesynssvakhet de har:

_____

_____

_____

_____

- Har dere forhørt dere om noen i deres nære familie har en fargesynssvakhet?

Ja, på mors side av familien ☐ Ja, på fars side av familien ☐ Nei ☐

Evt. kommentarer_____

_____

Vi anbefaler at dere, i den grad det lar seg gjøre, informerer de enkelte familiemedlemmene om at opplysninger om deres fargesyn er gitt.

1

HØGSKOLEN

Basert på opplysninger fra spørreskjemaet kan det være behov for å teste fargesynet til deres barn og den av de foresatte som fargesynssvakheten er nedarvet fra. Hvis dette er tilfelle, ber vi deg om å om å gi oss tillatelse til å kontakte dere ved å fylle ut skjemaet nedenfor.

En fargesynssvakhet er nedarvet via X-kromosomet, slik at en jente som er bærer vil ha arvet dette fra sin biologiske far om han er fargesvak, men kan også ha arvet det fra sin biologiske mor om hun er bærer. En jente som er fargesvak vil vanligvis ha en biologisk far som er fargesvak og en biologisk mor som er bærer. En gutt som er fargesvak vil ha arvet det fra sin biologiske mor som da vil være bærer.

Ja, dere kan ta kontakt med oss ☐

Nei, vi ønsker ikke å bli kontaktet ☐

Hvis Ja, vennligst fyll ut følgende kontaktinformasjon:

Kontaktinformasjon:

Datters/sønns navn:_____

Foreldre/foresattes navn:_____

Adresse:_____

_____

_____

Tlf.nr:_____

E-mailadresse:_____

VENNLIGST RETURNER FERDIG UTFYLT SPØRRESKJEMA I VEDLAGTE ADRESSERTE OG FRANKERTE KONVOLUTT.

Questionnaire female optometry students

SPØRRESKJEMA TIL KVINNELIGE OPTOMETRISTUDENTER

Fødselsår: _____

- Har du testet fargesynet ditt tidligere?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

- Har du en kjent fargesynssvakhet (ofte kalt fargeblindhet eller rød-grønn fargeblindhet)?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

- Har du problemer med å skille noen farger fra hverandre?

Ja ☐ Nei ☐ Vet ikke/usikker ☐

Hvis ja, hvilke farger:

_____

- Har noen i din nære familie en kjent fargesynssvakhet, og i så fall hvem?

Ja ☐ Nei ☐ Vet ikke ☐

Hvis Ja, vennligst noter nedenfor hvem (far/mor/bror/morfar/onkel/fetter etc.) og om disse familiemedlemmene hører til på mors eller fars side av familien. Dersom kjent, er det fint om dere noterer hvilken fargesynssvakhet de har:

_____

_____

_____

_____

- Har dere forhørt dere om noen i deres nære familie har en fargesynssvakhet?

Ja, på mors side av familien ☐ Ja, på fars side av familien ☐ Nei ☐

Evt. kommentarer_____

_____

Vi anbefaler at dere, i den grad det lar seg gjøre, informerer de enkelte familiemedlemmene om at opplysninger om deres fargesyn er gitt.

HØGSKOLEN

Basert på opplysninger fra spørreskjemaet kan det være behov for å teste fargesynet til den av dine foreldre som fargesynssvakheten er nedarvet fra, eventuelt andre familiemedlemmer. Hvis dette er tilfelle, ber vi deg om å om å gi oss tillatelse til å kontakte deg ved å fylle ut skjemaet nedenfor.

En fargesynssvakhet er nedarvet via X-kromosomet, slik at en jente som er bærer vil ha arvet dette fra sin biologiske far om han er fargesvak, men kan også ha arvet det fra sin biologiske mor om hun er bærer. En jente som er fargesvak vil vanligvis ha en biologisk far som er fargesvak og en biologisk mor som er bærer. En gutt som er fargesvak vil ha arvet det fra sin biologiske mor som da vil være bærer.

Ja, dere kan ta kontakt med meg ☐

Nei, jeg ønsker ikke å bli kontaktet ☐

Hvis Ja, vennligst fyll ut følgende kontaktinformasjon:

Kontaktinformasjon:

Navn:_____

Adresse:_____

_____

_____

Tlf.nr:_____

E-mailadresse:_____

VENNLIGST RETURNER FERDIG UTFYLT SPØRRESKJEMA I VEDLAGTE KONVOLUTT TIL ELISE WIKEN DEES SIN POSTHYLLE PÅ AVDELINGEN.

Appendix F

Scoring sheet

REGISTRERINGSSKJEMA FOR DELTAKELSE I FORSKNINGSPROSJEKT Samtykkeerklæring skal være underskrevet før registreringsskjema fylles ut.			
Dato:	Fødselsår:	○ Kvinne ○ Mann	Kode:
Navn:			
Avdeling: (for ansatte/studenter ved HiBu)			
Adresse:			
E-postadresse:			
Telefon dagtid:		Mobil:	

Dato:	Fødselsår:	Kode:		
Etnisk bakgrunn:			**Kvinne:**	**Mann:**
Dominant øye:			**Alder:**	

Habituell brillekorreksjon (visus testes med fullkontrast logMAR-tavle på 6,0 m):

HØ sphere	cyl	axis	**VA:**	**VØ** sphere	cyl	axis	**VA:**	**Bin VA:**
Add:				**Add:**				

Type brille (enstyrke/flerstyrke, hvite/fargetone, bruksområder):

Habituell kontaktlinsekorreksjon (visus testes med fullkontrast logMAR-tavle på 6,0 m):

HØ sphere	cyl	axis	**VA:**	**VØ** sphere	cyl	axis	**VA:**	**Bin VA:**

Type kontaktlinser (produktmerke, enstyrke/flerstyrke, hvite/fargetone/håndteringsfarge, bruksområder):

HISTORIE

Har du testet fargesynet ditt tidligere?
(når, med hvilke tester)

Har du en fargesynssvakhet?
(type, grad, når ble den oppdaget, symptomer)

Har du problemer med å skille noen farger fra hverandre?
(hvilke farger, når)

Finnes det fargesynssvakheter i din familie (dvs. hos oldeforeldre, besteforeldre, foreldre, søsken, barn, onkler, tanter, kusiner, fettere)? (type, grad, når ble den oppdaget, symptomer, familieforhold)
Har du eller har du hatt øyeskader, øyesykdommer eller andre sykdommer som kan påvirke synet/øynene? (f.eks. diabetes, optisk nevritt, grønn- eller grå stær)
Bruker du noen medisiner? (type, hyppighet, mengde)
Har du vært ute i sollys i dag? (varighet, bruk av solbriller)
Annet som kan være viktig for studien: (f.eks: familiekart ved fargesynssvakheter i familien)

RESULTATER PÅ FARGESYNSTESTER	**KODE:**			
NTCV (Bin) Dato: (/ /)	Ark nr.:		Ark nr.: (Retest)	
Lyskilde: *Dagslys &* *fluoriserende lysstoffrør.*	Feil rute nr:		Feil rute nr:	
Type defekt:	Protan / deutan / tritan / unspecified			
Behavior:	B1 / B2 / B3			
Ishihara 24 pl. (Bin) Dato: (/ /)	Antall plater lest som normal av pl. 1-15:			
Lyskilde: *True Daylight Ill. 6200 K*	Indikasjon (pl. 16-17)			
HRR 4th ed. (Bin) Dato: (/ /)		Tritan B/Y defekt	Protan/deutan R/G defekt	
Lyskilde: *True Daylight Ill. 6200 K*	Screening	Pl. 5-6	Pl. 7-10	
	Diagnostisk	Pl. 21-24	Pl. 11-20	
Type defekt:	Protan / deutan / tritan		Mild / medium / sterk	
FM100Hue (Bin) Dato: (/ /)	Feilscore: Normal feilscore for alderen:		Midpunkt - cap: Forvirringsakse:	
Lyskilde: *Sol Source D65*	Har du blitt testet med denne tidligere? Dato: (/ /)			
Medmont C-100 Dato: (/ /)	Blandingsratio:	1	2	3	4
HØ / VØ Type defekt:	Protan / deutan / normal trikromat Dikromat / anomal trikromat				
Medmont C-100 Dato: (/ /)	Blandingsratio:	1	2	3	4
HØ / VØ Type defekt:	Protan / deutan / normal trikromat Dikromat / anomal trikromat				

CCT	Trivector				Ellipse		
HØ / VØ / Bin	Datafil:				Datafil		
	Protan	Deutan	Tritan		1	2	3
Dato: (/ /)				Length			
2-16 cd/m2				Axis ratio			
				Angle			
Rombelysning: Av / på				Defect set: O Normal / O Tritanopic			

Kode	Dato	Testøye O HØ / O VØ

O Rayleighmatch / O Morelandmatch
Absolutt - Manuell

Standardmatch

Fargene oppleves: O Like / O Ulike	Farge på: Øverst: Nederst:	Egen fargematch: Aq: M: V:

Kontroll av matchingrange

Fargeblandinger til VENSTRE for matchingpunkt				**Fargeblandinger til HØYRE for matchingpunkt**		
Farge- blanding:	Like/ ulike:	Kommentar:		Farge- blanding:	Like/ ulike:	Kommentar:
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	
	O Like O Ulike				O Like O Ulike	

O Rødgrønnmatch **O Blågrønnmatch**
Endelig resultat

O HØ / O VØ	Resultat:	Kommentar
M1 - M2: V1 - V2: Aq1 -Aq2:		

Appendix G

Information letter to rectors

HØGSKOLEN
i Buskerud

Kongsberg, 17. september 2009

Informasjon angående studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter"

Viser til hyggelig telefonsamtale i går, 16. september. Legger ved konvoluttene som skal deles ut, barnas navn er skrevet på konvoluttene. Legger også ved dokumentene til deg, slik at du ser hva som sendes ut. Konvoluttene inneholder informasjonsbrev til foreldre, informasjons- og samtykkefolder, spørreskjema og ferdig frankert svarkonvolutt. Elevene tar med denne konvolutten hjem til sine foreldre. Spørreskjema og samtykkeerklæring returneres direkte til oss i den ferdig frankerte konvolutten, slik at dette ikke er noe dere skal administrere. Ut i fra svarene på spørreskjemaene velger vi hvem som skal delta i studien.

Svarfristen er satt til 1. oktober, så nøyaktig antall deltakere vet vi først noen dager etter denne datoen. Jeg ringer og avtaler endelig angående rom som kan mørklegges samt tidspunkt for testing og antall som skal testes når avtalt testtidspunkt nærmer seg.

Avtalte testtidspunkt er: **xxxdag xx., xxxdag xx. og xxxdag xx. november, uke xx**

Spørsmål kan rettes til Elise Wiken Dees eller Rigmor C. Baraas.

Takk for at dere lar oss gjennomføre studien på deres skole.

Vennlig hilsen

Rigmor C. Baraas (veileder)
Førsteamanuensis
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg

e-post: rigmor.baraas@hibu.no
Telefon: 32 86 97 87

Elise Wiken Dees (MPhil student)
Vitenskapelig assistent
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg

e-post: elise.wiken.dees@student.hibu.no
Telefon: 32 86 97 27 / 45 85 34 25

Information letter to normal trichromatic girls

HØGSKOLEN
i Buskerud

Kongsberg, 17. september 2009

Invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter"

Du/dere mottar dette brevet som en invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter". Våren 2006-07 ble fargesynet til deres datter testet av avgangselever ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap. Resultatene fra testene viser at hun har normalt fargesyn. Vi vil høsten 2009 utføre en oppfølgingsstudie, og ønsker derfor at du/dere tar deg/dere tid til å fylle ut vedlagte spørreskjema og samtykkeerklæringer.

Vennligst returner de GULE arkene i vedlagte frankerte konvolutt innen **1. oktober 2009**.

Vennligst les vedlagte informasjonsskriv for mer informasjon om studien. Spørsmål kan rettes til Elise Wiken Dees eller Rigmor C. Baraas.

Vennlig hilsen

Rigmor C. Baraas (veileder)
Førsteamanuensis
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
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3603 Kongsberg

e-post: rigmor.baraas@hibu.no
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Elise Wiken Dees (MPhil student)
Vitenskapelig assistent
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg

e-post: elise.wiken.dees@student.hibu.no

Information letter to colour deficient boys, Notodden and Bø

HØGSKOLEN
i Buskerud

Kongsberg, 17. september 2009

Invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter"

Du/dere mottar dette brevet som en invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter". Våren 2007 ble fargesynet til deres sønn testet av avgangselever ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap. Resultatene fra testene viser at han kan være rød-grønn fargesvak. Vi vil høsten 2009 utføre en oppfølgingsstudie, og ønsker derfor at du/dere tar deg/dere tid til å fylle ut vedlagte spørreskjema og samtykkeerklæringer.

Vennligst returner de GULE arkene i vedlagte frankerte konvolutt innen **1. oktober 2009**.

Vennligst les vedlagte informasjonsskriv for mer informasjon om studien. Spørsmål kan rettes til Elise Wiken Dees eller Rigmor C. Baraas.

Vennlig hilsen

Rigmor C. Baraas (veileder)
Førsteamanuensis
Avdeling for optometri og synsvitenskap
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Elise Wiken Dees (MPhil student)
Vitenskapelig assistent
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg

e-post: elise.wiken.dees@student.hibu.no

Information letter to colour deficient boys, Kongsberg

HØGSKOLEN
i Buskerud

Kongsberg, 17. september 2009

Invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter"

Du/dere mottar dette brevet som en invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter". Deres sønn deltok i fargesynsscreening våren 2006, eller skolescreening av syn i Kongsberg kommune i januar 2008-09, utført av Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap. Resultatene fra testene viser at deres sønn kan være rød-grønn fargesvak. Vi vil høsten 2009 utføre en oppfølgingsstudie, og ønsker derfor at du/dere tar deg/dere tid til å fylle ut vedlagte spørreskjema og samtykkeerklæringer.

Vennligst returner de GULE arkene i vedlagte frankerte konvolutt innen **1. oktober 2009**.

Vennligst les vedlagte informasjonsskriv for mer informasjon om studien. Spørsmål kan rettes til Elise Wiken Dees eller Rigmor C. Baraas.

Vennlig hilsen

Rigmor C. Baraas (veileder)
Førsteamanuensis
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
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3603 Kongsberg

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Elise Wiken Dees (MPhil student)
Vitenskapelig assistent
Avdeling for optometri og synsvitenskap
Høgskolen i Buskerud
Postboks 251
3603 Kongsberg

e-post: elise.wiken.dees@student.hibu.no

Information letter to carriers

HØGSKOLEN
i Buskerud

Kongsberg, 17. september 2009

Invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter"

Du/dere mottar dette brevet som en invitasjon til å delta i studien "Kartlegging av kvinnelige bærere av rød-grønne fargesynssvakheter". Våren 2006-07 ble fargesynet til deres datter testet av avgangselever ved Høgskolen i Buskerud, Avdeling for optometri og synsvitenskap. Resultatene fra testene er noe usikre og viser at hun kan være rød-grønn fargesvak, eller muligens at hun er bærer av en rød-grønn fargesynssvakhet. Vi vil høsten 2009 utføre en oppfølgingsstudie, og ønsker derfor at du/dere tar deg/dere tid til å fylle ut vedlagte spørreskjema og samtykkeerklæringer.

Vennligst returner de GULE arkene i vedlagte frankerte konvolutt innen **1. oktober 2009**.

Vennligst les vedlagte informasjonsskriv for mer informasjon om studien. Spørsmål kan rettes til Elise Wiken Dees eller Rigmor C. Baraas.

Vennlig hilsen

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Appendix H

Variables colour vision

Measurement	Definition	Measurement category	Explanation	Definition category
Id. nr.		Interval	Subjects are given identification number to ensure the anonymity	001, 002… etc.
Relationship	Code for father or mother, followed by their child's code	Nominal	The subjects relationship to another subject (parents and children)	0. Child 1. Mother 2. Father
Year of birth		Interval		1995, 1996… etc.
Age		Interval	Age when tested	20, 21, 22… etc.
Sex	Male Female	Nominal	Influence measurements	0. Male 1. Female
Ethnicity	Caucasian Asian African Spanish/Latin American Other	Nominal	Outcome measurements	3. Caucasian 4. Asian 5. African 6. Spanish/Latin America 7. Other
Eye dominance	Right eye Left eye	Nominal		0. RE 1. LE
Need of correction		Nominal	The subjects need of correction of refractive blur, specified spherical-cylindrical equivalence, contact lenses or glasses	0. No 1. Yes, all the time 2. Yes, during close up work 3. Yes, during distance work
Known eye injury		Nominal	Earlier eye injuries may affect the vision	0. No 1. Yes
Known eye disease		Nominal	Some eye diseases affect the colour vision	0. No 1. Yes

Known systemic disease		Nominal	Some systemic diseases affect the colour vision	0. No 1. Yes
Use of medicine		Nominal	Some medicines affect the colour vision	0. No 1. Yes
Hours spent in sunshine before the tests are carried out		Interval	Larger amount of sun light might affect the results of colour vision testing	0, 1, 2… etc…
NTCV sheet number		Interval	Three different NTCV sheets are available	1, 2 or 3
Number of errors on NTCV		Interval	Number of errors and specified which panel(s) mistaken	0, 1, 2… etc.
Retested NTCV sheet number		Interval	Subjects retested with another sheet number of the NTCV than they were tested with the first time	1, 2 or 3
Number of errors on retest NTCV		Interval	Number of errors and specified which panel(s) mistaken	0, 1, 2… etc.
Diagnose NTCV	Normal trichromacy Behaviour 1 Behaviour 2 Behaviour 3 Tritan behaviour 1 Tritan behaviour 2 Unclassified	Ordinal	 Strong Moderate Strong Moderate Strong	0. Normal 1. B1 2. B2 3. B3 4. TB1 5. TB2 6. Unclassified
Number of errors on Ishihara		Interval	Plates read correctly: >12 – normal colour vision <10 red-green deficiency	0, 1, 2… etc.
Degree, Ishihara	Normal trichromacy	Ordinal	 Moderate	1. Normal 2. P1

	Protan 1 Protan 2 Deutan 1 Deutan 2 Unclassified		Strong Moderate Strong	3. P2 4. D1 5. D2 6. Unclassified
Number of errors screening plates HRR 2002		Interval	One or more plates read incorrectly: The subjects are retested	0, 1, 2… etc.
Number of errors retest screening plates HRR 2002		Interval	Two or more errors: Probably colour deficient subject	0, 1, 2… etc.
Specified which screening plate(s) mistaken		Interval	Blue-yellow plates Red-green plates	Plate 5, 6… etc. Plate 7, 8… etc.
Specified which diagnostic plate(s) mistaken		Interval	Blue yellow plates Red-green plates	Plate 21, 22… etc. Plate 11, 12… etc.
Diagnose HRR 2002	Normal Protan Deutan Tritan Tetartan Unclassified	Ordinal	All plates read correct Red-green plates red incorrectly Blue-yellow plates red incorrectly	0. N 1. P 2. D 3. T 4. TT 5. U
Behaviour HRR 2002	Normal Mild Medium Strong	Ordinal		0. N 1. Mild 2. Medium 3. Strong
Error score FM100-Hue	Total error scores Total partial error scores, red-green Total partial error scores, blue-yellow	Interval	Caps: 13-33, 55-75 Caps: 1-12, 34-54, 76-85	0, 1, 2… etc.
Expected upper limit error score for different ages		Interval	Upper error score for each age tested with FM100-Hue	76, 77, 78… etc.
Midpoint cap		Interval		0, 1, 2… etc.

Below or over the 95% confidence level		Nominal		0. Below 1. Over
Tested FM100-Hue earlier, and how many months ago		Interval	Subjects tested before are expected to perform better than first time	0, 1, 2… etc
Mixture ratio Medmont C-100		Interval	Mean value, between -5,0 and +5,0, right and left eye separately	-5, -4, -3… etc.
Degree, Medmont C-100	Normal trichromacy Protan Deutan	Nominal	Normal (-1,49 to +1,49) Protan (-5 to -1,5) Deutan (+1,5 to +5)	0. N 1. P 2. D
Trivector test CCT	Protan Deutan Tritan	Interval	Values of three different axis	0, 1, 2… etc
Behaviour trivector CCT	Normal trichromasy Protan Deutan Tritan Unclassified	Nominal	Outcome measurement	1. N 2. P 3. D 4. T 5. U
Ellipse CCT	Length Axis ratio Angle	Interval	Outcome measurement	0,001, 0,002… etc 1,0, 1,1… etc 50, 51… etc
Rayleigh match	Aq matching point Match midpoint Reference light match point Matching range Geometrical midpoint	Interval	Outcome measurement	0 to ∞ 0-73 0-45 0-73 0-73
Diagnose Rayleigh match	Normal trichromacy Protanomaly Strong protanomaly Protanope Deuteranomaly	Nominal	 Anomalous trichromacy Dichromacy Anomalous trichromacy Dichromacy	1. N 2. PA 3. EPA 4. P 5. DA 6. EDA 7. D

	Strong deuteranomaly Deuteranope Achromatopsia Diagnosis not possible			8. A 9. DNP
Moreland match	Aq matching point Match midpoint Reference light match point Matching range Geometrical midpoint	Interval	Outcome measurement	0 to ∞ 0-100 0-100 0-100 0-100
Diagnose Moreland match	Normal trichromacy Tritanope Achromatopsia Diagnosis not possible	Nominal	Outcome measurement	0. N 1. T 2. A 3. DNP

Variables questionnaire

Measurement	Definition	Measurement category	Explanation	Definition category
Year of birth		Interval		1995, 1996… etc.
Sex	Male Female	Nominal	Influence measurement	Influence measurements
Colour vision tested before this study		Nominal	Many colour deficient have never had their colour vision checked	0. No 1. Yes 2. Uncertain
Certainty of possible colour vision deficiency		Nominal	Many people do not know they are colour deficient	0. No 1. Yes 2. Uncertain
Problems with colour discriminations		Nominal	Colour coding can give colour deficient subjects daily problems	0. No 1. Yes 2. Uncertain
Members of the family with colour deficiencies		Nominal	Surveying carriers	0. No 1. Yes 2. Uncertain
Carrier of red-green colour vision deficiency		Nominal	Surveying carriers	0. No 1. Yes 2. Uncertain

Appendix I

Moreland match midpoints

Descriptives

Geometrical midpoint

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
0	29	53.5293	4.17068	.77448	51.9429	55.1158	45.50	61.00
3	32	52.3359	3.54026	.62584	51.0595	53.6123	44.30	59.60
Total	61	52.9033	3.86706	.49513	51.9129	53.8937	44.30	61.00

Figure 7-1 Appendix F Moreland match midpoints, descriptive statistics. Group 0 were tested with field size of 2°, group 3 were tested with 4°.

ANOVA

Geometrical midpoint

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	21.666	1	21.666	1.460	.232
Within Groups	875.584	59	14.840		
Total	897.249	60			

Figure 7-2 Appendix F Moreland match midpoints, ANOVA, no significant difference in null-point settings between groups 0 and 3. Group 0 were tested with field size of 2°, group 3 were tested with 4°.

Appendix J

The carriers' individual scores on the different tests

No.	Age	Type of possessed deficiency	# of misreadings NTCV	Diagnosis NTCV	# of misreadings Ishihara	Diagnosis Ishihara	# of misreadings screening HRR 2002	# of misreadings retest HRR 2002	Diagnosis HRR 2002	Behaviour HRR 2002
091	9	Protan	-	Normal	3	Unclassified	-	-	Normal	-
092	10	Protan	-	Normal	-	Normal	-	-	Normal	-
114	36	Protan	-	Normal	-	Normal	-	-	Normal	-
081	37	Protan	-	Normal	-	Normal	-	-	Normal	-
146	38	Protan	-	Normal	1	Normal	2	-	Normal	-
131	39	Protan	-	Normal	2	Normal	3	2	Unclassified	Unclassified
166	39	Protan	-	Normal	-	Normal	2	-	Normal	-
134	41	Protan	-	Normal	-	Normal	-	-	Normal	-
074	9	Deutan	2	Deutan B2	2	Normal	2	-	Normal	-
098	9	Deutan	-	Normal	3	Unclassified	2	-	Normal	-
077	11	Deutan	-	Normal	1	Normal	-	-	Normal	-
123	11	Deutan	1	Deutan B1	8	Unclassified	2	2	Unclassified	Unclassified
136	12	Deutan	-	Normal	1	Normal	2	-	Protan	Mild
019	20	Deutan	-	Normal	-	Normal	-	-	Normal	-
033	20	Deutan	-	Normal	1	Normal	-	-	Normal	-
062	20	Deutan	-	Normal	-	Normal	-	-	Normal	-
012	25	Deutan	-	Normal	-	Normal	-	-	Normal	-
097	32	Deutan	2	Red-green B1	1	Normal	-	-	Normal	-
133	37	Deutan	-	Normal	-	Normal	-	-	Normal	-
168	38	Deutan	-	Normal	3	Unclassified	-	-	Normal	-
157	39	Deutan	1	Deutan B1	3	Unclassified	2	-	Normal	-
038	41	Deutan	-	Normal	-	Normal	-	-	Normal	-
135	41	Deutan	-	Normal	1	Normal	-	-	Normal	-
161	43	Deutan	-	Normal	2	Normal	-	-	Normal	-
073	44	Deutan	-	Normal	4	Unclassified	2	-	Normal	-
163	45	Deutan	1	Unclassified	-	Normal	2	-	Normal	-
165	45	Deutan	1	Unclassified	2	Normal	-	-	Normal	-
132	51	Deutan	-	Normal	2	Normal	2	2	Unclassified	Unclassified
129	54	Deutan	-	Normal	-	Normal	2	2	Unclassified	Unclassified
036	66	Deutan	1	Deutan B1	1	Normal	-	-	Normal	-

No.	Age	Type of possessed deficiency	TES FM100-Hue	Expected age matched TES	FM100-Hue Mid-point cap	SQRT TES FM100-Hue	FM100-Hue Angle	FM100-Hue Selectivity index	FM100-Hue Confusion index	Null-point Medmont C-100
091	9	Protan	171	310	51	13,076697	-61,4	1,06	2,16	-1,81
092	10	Protan	65	260	13	8,0622577	63,2	1,08	1,34	-1,75
114	36	Protan	131	80	42	11,445523	55	1,45	2,08	-3,38
081	37	Protan	66	80	48	8,1240384	71,1	1,29	1,44	-3,88
146	38	Protan	131	80	60	11,445523	34,4	1,37	1,99	-3,25
131	39	Protan	126	80	76	11,224972	51,3	1,64	2,04	-1,44
166	39	Protan	67	80	47	8,1853528	-86,9	1,46	1,55	-3,19
134	41	Protan	28	100	30	5,2915026	55,9	1,36	1,24	-2,69
074	9	Deutan	136	310	28	11,661904	35,5	1,38	1,94	0,25
098	9	Deutan	111	310	31	10,535654	56,4	1,47	1,9	-1,75
077	11	Deutan	321	220	55	17,916473	33,1	1,09	2,96	-0,94
123	11	Deutan	416	220	57	20,396078	-88,3	1,19	3,5	-0,50
136	12	Deutan	63	180	80	7,9372539	50	1,5	1,55	-0,63
019	20	Deutan	75	76	83	8,660254	63,1	1,52	1,72	-2,94
033	20	Deutan	100	76	51	10	-83,7	1,37	1,8	-2,06
062	20	Deutan	111	76	14	10,535654	46,9	1,23	1,8	-2,69
012	25	Deutan	78	78	55	8,8317609	50,1	1,2	1,42	-2,19
097	32	Deutan	91	80	46	9,539392	72,9	1,51	1,78	0,25
133	37	Deutan	63	80	47	7,9372539	88,7	1,34	1,45	-0,94
168	38	Deutan	138	80	65	11,74734	50,8	1,27	1,83	-1,75
157	39	Deutan	118	80	56	10,86278	-53	1,2	1,83	-1,44
038	41	Deutan	70	100	3	8,3666003	72,2	1,3	1,51	-0,69
135	41	Deutan	38	100	32	6,164414	51,4	1,26	1,2	-1,75
161	43	Deutan	48	100	34	6,9282032	47,2	1,52	1,5	-0,31
073	44	Deutan	56	100	79	7,4833148	53,3	1,46	1,43	-0,63
163	45	Deutan	245	100	38	15,652476	54,5	1,33	2,6	-1,19
165	45	Deutan	88	100	51	9,3808315	66,6	1,23	1,65	-0,94
132	51	Deutan	181	130	37	13,453624	52,9	1,69	2,48	-1,06
129	54	Deutan	256	136	41	16	54,7	1,39	2,71	-2,06
036	66	Deutan	67	170	55	8,1853528	54,5	1,07	1,33	-0,94

No.	Age	Type of possessed deficiency	CCT Trivector protan axis	CCT Trivector deutan axis	CCT Trivector tritan axis	CCT Ellipse length	CCT Ellipse axis ratio	CCT Ellipse angle	Rayleigh match midpoint	Rayleigh matching range	Rayleigh match luminance	Moreland match midpoint	Moreland matching range	Moreland match luminance
091	9	Protan												
092	10	Protan												
114	36	Protan							38,2	3,2	12,65	52,9	0	43,1
081	37	Protan							42,65	2,3	11,7	50	0	44,3
146	38	Protan							42,1	1,2	14,55	54,9	6,2	44,5
131	39	Protan							41,2	4	13,05	45,3	8,2	39,25
166	39	Protan	81	93	106	0,0252	1,28	89,4	42,95	2,7	13,3	50	5	43,75
134	41	Protan							41,2	4	12,7	51,2	8,2	44,75
074	9	Deutan												
098	9	Deutan												
077	11	Deutan												
123	11	Deutan												
136	12	Deutan												
019	20	Deutan	62	81	91	0,0227	1,13	51,5	39,45	1,1	14,65	62,95	9,1	53,45
033	20	Deutan	66	60	75	0,0159	1,22	45,8	39,95	3,7	14,8	49,6	2,8	44,1
062	20	Deutan	66	62	67	0,0143	1,16	49,9	39,65	1,5	14,3	50,5	1	43,5
012	25	Deutan	55	56	76	0,0156	1,28	81	39,85	5,1	13,95	48,45	23,1	44,3
097	32	Deutan	74	89	93	0,0158	1,21	171,8	37,2	1,2	15,2	54,7	2	48,2
133	37	Deutan							39,25	1,7	13,5	50,2	3,2	42,55
168	38	Deutan							38,8	3,2	14,2	51,25	2,5	43,1
157	39	Deutan	102	62	92	0,0193	1,22	34,3	42,35	1,1	13,15			
038	41	Deutan	81	121	108	0,0173	1,12	60,4	39,9	2	12,15	58,05	36,1	51,2
135	41	Deutan							43,05	1,1	16,3			
161	43	Deutan							34,65	1,7	15	50,8	6,6	49,45
073	44	Deutan							39,5	4,6	14,75	44,15	5,1	40,15
163	45	Deutan							34,95	1,1	14,9	32,75	12,9	35,7
165	45	Deutan							35,65	0,9	13,8	47,95	4,1	45
132	51	Deutan							37,5	1,8	13,25	57,25	7,1	48,2
129	54	Deutan							38,2	1,4	15,25	37,25	7,1	25,9
036	66	Deutan	256	144	182	0,0306	1,29	146,5						