

**C. Erb<sup>1,\*</sup>**, **B. Weisser<sup>2</sup>**<sup>1</sup>Private Institute of Applied Ophthalmology Berlin, Berlin, Germany<sup>2</sup>Department of Sportsmedicine, Christian-Albrechts-University, Kiel, Germany\*e-mail: [erb.glaukom@gmail.com](mailto:erb.glaukom@gmail.com)

## SIGNIFICANCE OF ACQUIRED COLOR VISION DEFECTS IN THE DIAGNOSIS OF VASCULAR DISEASES

Color vision testing can be used to detect subtle disturbances in retinal function, which can often occur before clinical symptoms and, for the ophthalmologist, before visible changes in the fundus of the eye in general vascular diseases. This makes it possible to carry out rapid and inexpensive early diagnosis by detecting acquired color vision disorders, which can prevent further damage by optimizing therapy. Here it is particularly important to work closely with general practitioners and internists. Such aspects should be given greater consideration in occupational medicine. In many areas of industry, high demands are placed on color vision. In areas such as the textile industry, the chemical paint industry, the food industry, the automotive industry (paints) and in painting companies, normal color perception is of fundamental importance. Color vision testing is an inexpensive and easy-to-perform examination method that can provide an early indication of acquired color vision deficiency under standardized conditions. In addition to the detection of a generalized microcirculatory disorder, this determination is also useful in occupational medicine in order to better determine suitability for certain occupational groups.

**Key words:** color vision, vascular diseases, diabetes, arterial hypertension, migraine.

### Introduction

The eye is supplied by the ophthalmic artery as a branch of the internal carotid artery. The central artery is responsible for supplying the inner retinal layers and is subject to autoregulation [1], which ensures a constant blood flow as long as the average arterial blood pressure does not vary by more than 40% [2].

### Material and Methods

This study is an evaluation review. The literature was searched in the databases PubMed, Scopus, Web of Science, Springer. Duplicate publications have been checked and deleted. Initially, 83 articles were identified. After removing duplicates, 57 publications remained (26 excluded) as a result of searching in electronic databases and viewing links to articles. The application of inclusion/exclusion criteria and a thorough study of the abstracts led to the exclusion of 21 studies. Of the remaining 36 articles, 5 were excluded for the following reasons: 4 – there is no complete text, 1 – questionable methods of statistical analysis. The rest of the studies were suitable for qualitative synthesis.

### Results and Discussion

The choroid is mainly fed by the short posterior ciliary arteries, and supplies per diffusionem the outer retinal layers with the photoreceptors (cones, rods) up to the retinal pigment epithelium as well as the anterior part of the optic nerve via ciliary (choroidal) arteries. The major portion of the blood from the ophthalmic artery, contributes to uveal circulation (85%) and only 2-5% goes to the retinal vasculature [3]. Due to the pronounced capillary network, the choroid has the largest blood volume in proportion to the perfused tissue weight in the entire body with a blood flow volume of 18 ml/min/g tissue [4]). It also appears to have autoregulation [5], although this is far less effective than retinal autoregulation.

Due to the size of the retinal and choroidal vessels below 300  $\mu\text{m}$ , ocular perfusion is part of the microcirculation. If systemic diseases lead to a disturbance of the microcirculation, microvascular dysfunction is considered a systemic disease [6], as it then generally affects all organ systems, including ocular perfusion. As this can affect the retinal photoreceptors, color vision is also a sensitive marker for microcirculatory disorders.

Color vision is one of the most highly developed human senses. It is made possible by the 3 photoreceptors (green, red and blue cones) in the retina and by cerebral processing [7,8].

Rhodopsin serves as a light sensor for incident light. It occurs as a photopigment in both the rods and the cones. Rhodopsin differs in the individual photoreceptor groups by slightly altered amino acid sequences in the opsin part, which causes the different wavelength sensitivity: rod rhodopsin has an absorption maximum around 500 nm (maximum sensitivity for green light), the cone rhodopsins have absorption maxima at 445 nm (blue cones), 545 nm (green cones) and 565 nm (red cones). They form the basis of color vision [9].

The three types of cones occur with different frequencies, the green cones are the most common with 55%, followed by the red cones with 33% and the blue cones with 12%. The blue cones only make up 2-3% of the color receptors in the fovea [10]. They are the youngest cones in evolutionary terms and react particularly sensitively to external factors [11].

As a result, the onset of acquired color vision disorders often begins with blue-yellow disorders with a typical color axis (Figure 1).

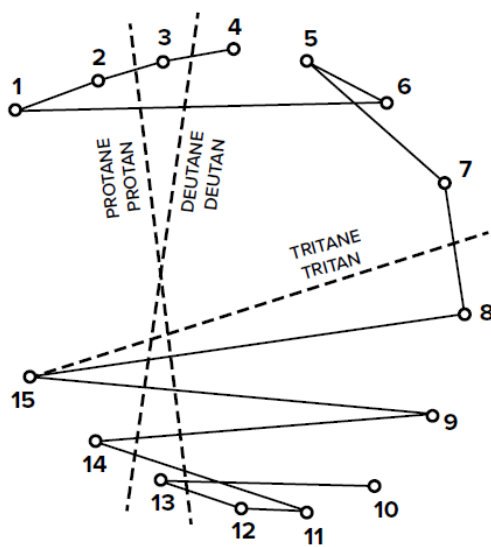


Figure 1 – Blue-yellow disorder in panel D 15 desaturated [31]

#### *Findings without a reliable color axis*

Acquired color vision deficits can, however, also be conspicuous by a “finding without a reliable axis” [12]. This is a dyschromatopsia without a preferred axis disorder. If there is also a low error sum, this indicates an incipient color vision disorder, which can later develop into a definite color vision disorder.

If there is a “finding without a reliable axis” with a very high error sum, this is an indication of a far advanced color vision disorder, in the course of which a generalized disorder of all photoreceptors has occurred.

Acquired color vision deficits can occur in the context of all general vascular diseases and indicate a microcirculatory disorder at an early stage [13]. This gives color vision testing a new dimension and significance in everyday clinical practice in the field of non-invasive early detection of vascular diseases, which can also be implemented easily and inexpensively.

#### *Difference between acquired and congenital color vision disorders*

Acquired color vision disorders generally differ from congenital color vision disorders in that they are highly variable, often begin unilaterally, are usually accompanied by conspicuous eye findings and are highly dependent on the examination conditions [14]. This shows that the examination conditions must be as standardized as possible in order to obtain reliable information, especially during the course of the disease [14]. A learning defect and the patient’s level of experience in handling colors must be taken into account [15]. It is also important to note that reliable qualitative and quantitative information can only be obtained with color pigment sample tests (e.g. Panel D 15 desaturated, Farnsworth 100-hue test) or with an anomaloscope with Rayleigh and Moreland equation. In addition, the anomaloscope should also have a 4° eyepiece instead of the usual 2° eyepiece in order to be able to better diagnose the low foveal blue cone density.

#### *Benefits of detecting acquired color vision defects*

In an earlier study, it was shown that ventilation with 10% oxygen results in a blue-yellow disorder and a “finding without a reliable axis” compared to normal breathing with 21% oxygen [16]. This is explained by an oxygen deficiency of the retinal ganglion cells. This basic experiment proved that, in principle, any type of circulatory disorder in the ocular microcirculation can lead to color vision defects. It is therefore quite possible to use the color sense test to make an indirect statement about the state of the microcirculation in the eye and as a representative of the general microcirculation.

#### *Acquired color vision deficits in vascular diseases*

Acquired color vision deficits have been demonstrated in patients with functional vascular disorders, such as in the free interval in sudden hearing loss [17] and migraine [18], as well as in vascular

diseases with structural remodeling processes in the vessels, such as arterial hypertension [19], diabetes mellitus [20,21] or coronary heart disease [22].

In diabetes mellitus, for example, a color vision disorder was detected before changes occurred in the fundus of the eye [23]. Typically, a blue-yellow disorder [24] or a “finding without a definite axis” occurs [25]. These findings are of general relevance. In the Early Treatment Diabetic Retinopathy Study, approximately 50% of patients with diabetic retinopathy had abnormal hue discrimination compared to published data on normal subjects. The severity of macular edema, age and the presence of new vessels were the factors most strongly associated with impaired color discrimination [26].

However, acquired color vision deficits also occur in hematologic diseases, such as pernicious anemia and acute myeloid leukemia, both of which can lead to vascular dysfunction [27,28,29]. In addition, acquired color vision defects also occur with elevated serum LDL cholesterol levels and are more pronounced the higher the LDL cholesterol levels are [30].

#### *Consequences of color vision deficits in the workplace*

In many areas of industry, high demands are placed on color vision. In areas such as the textile

industry, the chemical paint industry, the food industry, the automotive industry (paints) and in painting companies, normal color perception is of fundamental importance. However, if workers have general vascular diseases, their color perception can be significantly impaired. Although it has been shown that employees can compensate for part of their acquired color perception disorder through their color experience [15], this is no longer possible in the case of more severe general illnesses. Further studies are needed to better assess the effects of these color vision impairments in occupational medicine using standardized color vision tests [14].

#### **Conclusion**

Color vision testing is an inexpensive and easy-to-perform examination method that can provide an early indication of acquired color vision deficiency under standardized conditions. In addition to the detection of a generalized microcirculatory disorder, this determination is also useful in occupational medicine in order to better determine suitability for certain occupational groups.

#### **Acknowledgments**

No funding.

#### **References**

1. Bill A., Sperber G.O. (1990) Control of retinal and choroidal blood flow. *Eye*; 4:319-25
2. Robinson F., Riva C.E., Grunwald J.E., Petrig B.L., Sinclair S.H. (1986) Retinal blood flow autoregulation: a response to an acute increase in blood pressure. *Invest Ophthalmol*: 27:722-26
3. Bill A. (1975). Blood circulation and fluid dynamics in the eye. *Physiol Rev* 55: 383-417.
4. Alm A., Bill A. (1973) Ocular and optic nerve blood flow at normal and increased intraocular pressures in monkeys (*Macaca irus*): a study with radioactively labelled microspheres including flow determinations in brain and some other tissues. *Exp Eye Res*; 15:15-29.
5. Kiel J.W. Choroidal myogenic autoregulation and intraocular pressure. *Exp Eye Res* 1994; 58:529-43.
6. Feuer D.S., Handberg E.M., Mehrad B., Wei J., Bairey Merz C.N., Pepine C.J., Keeley E.C. (2022). Microvascular Dysfunction as a Systemic Disease: A Review of the Evidence. *Am J Med*. 2022 Sep;135(9):1059-1068. doi: 10.1016/j.amjmed.04.006. Epub Apr 23. PMID: 35472396; PMCID: PMC9427712.
7. Hofmann L., Palczewski K. (2015) Advances in understanding the molecular basis of the first steps in color vision. *Prog Retin Eye Res* 49: 46–66
8. Conway B.R. (2009) Color vision, cones, and color-coding in the cortex. *Neuroscientist* 15: 274–90
9. Hofmann L., Palczewski K. (2015) Advances in understanding the molecular basis of the first steps in color vision. *Prog Retin Eye Res*. Nov; 49:46-66. doi: 10.1016/j.preteyeres.2015.07.004. Epub 2015 Jul 15. PMID: 26187035; PMCID: PMC4651776.
10. Marc R.E., Sperling H.G. (1977). Chromatic organization of primate cones. *Science*. Apr 22;196(4288):454-6. doi: 10.1126/science.403607. PMID: 403607.
11. Zrenner E., Gouras P. (1981). Characteristics of the blue sensitive cone mechanism in primate retinal ganglion cells. *Vision Res*. 21(11):1605-9. doi: 10.1016/0042-6989(81)90042-0. PMID: 7336593.
12. Marré M., Marré E. (1986). *Erworbene Störungen des Farbsehen*. Leipzig, Thieme
13. Erb C., Schröder A., Krastel H. (2004) Farbsinnstörung – ein diagnostischer Hinweis auf vaskuläre Allgemeinerkrankungen? *Z prakt Augenheilkd* 25: 17–20
14. Erb C., Fahle M. (2006) Farbsehen und erworbene Farbsinnstörungen. Teil I: Grundlagen. *Ophthalmologe* 103: 349–360

15. Schröder A., Meinrencken J., Gockeln R., Erb C. (2002) Positiver Einfluss von Farberfahrung auf das Ergebnis von Farbsinnstörungen mit dem Farbpigmentprobentest Roth 28-hue (E) desaturiert. *Klin Monatsbl Augenheilkd* 219: 33–36
16. Smith V.C., Ernest J.T., Pokorny J. (1976) Effect of hypoxia on FM 100-Hue test performance. *Mod Probl Ophthalmol* 17: 248–256
17. Erb C., Preyer S., Thiel H.J. (1996) Ophthalmologische Befunde bei Patienten mit Hörsturz. *Ophthalmologe* 93: 433–439
18. Shepherd A.J. (2005) Colour vision in migraine: selective deficits for S-cone discriminations. *Cephalalgia* 25: 412–423
19. Schröder A. et al (2002) Farbsinnstörungen bei Patienten mit einer arteriellen Hypertonie. *Ophthalmologe* 99: 375–379
20. Chen X.D., Gardner T.W. (2021) A critical review: Psychophysical assessments of diabetic retinopathy. *Surv Ophthalmol* 66: 213–230
21. Safi H. et al (2018) Early detection of diabetic retinopathy. *Surv Ophthalmol* 63: 601–608
22. Erb C. E. et al (2001) Color-vision disturbances in patients with coronary artery disease. *Col Res Appl* 26: 288–291
23. Kurtenbach A. et al (1994) Brightness matching and colour discrimination in young diabetics without retinopathy. *Vision Res* 34: 115–122
24. Roy M., Gunkel R.D., Podgor M.J. (1986) Color vision defects in early diabetic retinopathy. *Arch Ophthalmol* 104: 225–228
25. Trick G.L. et al (1988) The relationship between hue discrimination and contrast sensitivity deficits in patients with diabetes mellitus. *Ophthalmology* 95: 693–698
26. Fong D.S., Barton F.B., Bresnick G.H. (1999) Impaired color vision associated with diabetic retinopathy: Early Treatment Diabetic Retinopathy Study Report No. 15. *Am J Ophthalmol* 128: 612–617
27. Chisholm I.A. (1972) The dyschromatopsia of pernicious anaemia. *Mod Prob Ophthalmol* 11: 130–135
28. Ziaei M. et al (2013) Acquired dyschromatopsia in acute myelocytic leukaemia. *Doc Ophthalmol* 127: 249–253
29. Talcott K.E., Garg R.J., Garg S.J. (2016) Ophthalmic manifestations of leukemia. *Curr Opin Ophthalmol* 27: 545–551
30. Shoji T et al (2010) Serum low-density lipoprotein cholesterol level is strong risk factor for acquired color vision impairment in young to middle-aged Japanese men: the Okubo Color Study Report 2. *Atherosclerosis* 210: 542–547
31. Tan A., Mallika P., Aziz S., Asok T., Intan G. (2008). Ethambutol ocular toxicity in a patient with pul-monary tuberculosis – a case report. *Malays Fam Physician*, Aug 31;3(2):87-90. PMID: 25606123; PMCID: PMC4170310.

*Significance-of-acquired-color-vision-defects-in-the-diagnosis-of-vascular-diseases*

**Information about authors:**

C. Erb – Director of Private Institute of Applied Ophthalmology Berlin, Berlin, Germany, e-mail: [erb.glaukom@gmail.com](mailto:erb.glaukom@gmail.com)

B. Weisser – Head of department of Sportsmedicine, Christian-Albrechts-University, Kiel, Germany

*Date of receipt of the article: May 26, 2024.*

*Accepted: July 17, 2024.*