Journal of Research Administration
Society of Research Administrators International

THE EFFECT OF VİSUAL PERCEPTİON REHABİLİTATİON ON FUNCTİONAL VİSİON İN CASES WİTH HEREDİTARY RETİNAL DYSTROPHY

H.Semrin Timlioğlu İPER MD.Ophthal.PhD[1,2]

ORCID :0000-0003-2112-0602 semrin.iper@okan.edu.tr

Fatime Nilüfer YALÇINDAĞ MD.Ophthal.Prof.[3]

ORCİD 0000-0002-8963-51-46 nil.yalcindag@gmail.com

1.İstanbul Okan University Hospital clinic of Ophthalmology

2.İstanbul Okan University Vocabulary school Opticianry

3.Unıversity of Ankara Medical school Clinic of Ophthalmology

ABSTRACT

Hereditary retinal dystrophies (HRD) are genetic diseases that cause progressive vision loss. They occupy an important place among the causes of low vision, especially in childhood. Vision loss, which begins in childhood, increases with age, and these people may become dependent on others with increasing vision loss. In recent years, the development of the concept of neuroplasticity and learning through experience has shown that rehabilitation can increase functional vision in hereditary retinal diseases. In this context, the aim of this study is to increase the visual skills and functional vision of people with low vision due to HRD/Cone Dystrophy (CD) and to create a beginning for the development of vision rehabilitation approaches that reduce the level of disability and increase participation in social production. The population of our study consists of 180 patients registered at Ankara University Ophthalmology Clinic, Low Vision Rehabilitation and Vision Research Center. The sample size was calculated as a minimum of 16 patients with 80% margin of power and 5% margin of error, and since CD was in the rare disease group, the pre-rehabilitation values of the patients were used as the control group. From the total population, 19 patients were randomly included in the study. Electroretinography (ERG) was used to confirm that the selected patient group had CD. In addition to visual acuity, refractive value measurement, anterior segment, fundus, and eye movements examinations, contrast sensitivity, Microperimetry, MVPT_4 test (Visual perception skills test), NVFQ-25 low vision quality of life scale, MNRead reading tests were applied. In rehabilitation applications, manual methods and the most commonly used digital device in this regard, Bernell Vision Trainer (OTSP1SO and OTSP1), were used. ICF coding was applied to all patients. As a result, visual rehabilitation applications were effective in functional vision levels and improving visual skills. It was found that they increased the quality of life.

Keywords: Hereditary Retinal Dystrophies, Cone Dystrophy, Neuroplasticity, Vision Rehabilitation, Quality of Life

INTRODUCTION

The most basic skills in the visual hierarchy are visual acuity, visual field and oculomotor control. At the second level, there are visual attention skills, which enable scanning and identifying the environment. The use of this set of skills as needed in various situations and environments in daily life is called functional vision (Collignon, Champoux, Voss, & Lepore, 2011; Parmeggiani et al., 2011). While the functioning of the structural elements of the visual system is called vision function, the ability to use visual skills in tasks in life is called functional vision. Even if their visual acuity is low, individuals whose functional vision is increased have less difficulty in accomplishing their daily tasks than individuals with the same visual acuity (Berardi, Sale, & Maffei, 2015). Moreover, getting an education, learning a profession, as well as independence in daily life needs depend on the ability to use functional vision skills, and even the lowest residual vision plays an important role in the development of these skills. Studies have shown that even in people with the same visual function level, there are differences in their use of their existing visual skills, that is, their visual skills, just like the differences seen in clinical pictures. The reason for this is that individuals' functional vision skills develop differently depending on their learning experiences and the environments they are in (Merabet and Pascual-Leone, 2010).

According to the World Health Organization (WHO) classification (Murray, Lopez, Mathers, & Stein, 2001, p. 36), patients whose visual acuity is less than zero and whose visual field is less than 20 degrees are called "low vision". In individuals with low vision, visual acuity often cannot be increased, and there is even a progressive loss in diseases such as hereditary retinal dystrophies (HRD). Difficulties in carrying out daily living activities and low ability to be active make people with low vision 15-30% more dependent on others than other disabled groups. Studies have shown that dependence rates are very high even in basic life activities such as shopping, using home medications without fail, making sure that the correct medication is taken, protecting from simple home accidents or coping with them if they occur, going up and down the stairs alone, and using public transportation (Burton et al., 2021; Aslan and Çakmak, 2016).

Hereditary retinal dystrophies (HRD) are used to describe a heterogeneous group of diseases of the neuroretina characterized by hereditary and genetic permanent retinal damage that can be transmitted through the entire Mendelian genetic pathways. The clinical picture they create depends on genotypic mutations, and different clinical pictures may occur even in different members of the same family (Birtel 2018). Due to genetic disorders, the functions of the photoreceptor cell layer and retinal pigment epithelium (RPE) are disrupted and progressive photoreceptor apoptosis occurs. Essentially, there are deficiencies in proteins involved in the visual cycle or phototransduction cascade, and today around 270 disease genes that cause HRD mutation have been identified. Hereditary retinal dystrophies (HRD) cause progressive vision loss and occupy an important place among the causes of low vision, especially in childhood. Cone Dystrophy (CD), on the other hand, is a rare genetic disease seen in HRD and is basically divided into two subtypes: stationary and progressive. While stationary cone disorders (cone dysfunction syndromes) begin congenitally/in early childhood and lead entirely to dysfunction of the cones, progressive cone dystrophies begin later and usually involve the rods. However, some forms of cone dysfunction syndrome, such as achromatopsia, occur in small numbers and may show limited progression over time (Georgiou 2021). A decrease in visual acuity and central visual sensitivity may manifest itself with some color vision deficiencies before becoming obvious (especially tritanopia). Nystagmus may not be observed in those whose cone function is initially normal. The onset of vision loss varies depending on the patient (adolescence-middle age). Apart from this, there are findings such as central scotoma, some color vision defects and hemeralopia. Unlike Retinitis pigmentosa (RP), which is rod-cone dystrophy, pigment deposits can be seen in the macula instead of the peripheral retina (Yu, 2022). The earliest electroretinography (ERG) finding in CD is the delayed 30 Hz flicker ERG implicit time, which selectively evaluates the cone response. This is followed by decay of the 30 Hz ERG amplitude and reduction of the a-wave and b-wave amplitudes of the photopic flash ERG. In early disease, scotopic function is preserved, but in the late stage it is usually affected (Gill 2018).

In studies conducted to enable people with low vision to participate in social life and create individual autonomy, it is seen that visual perception training increases people's functional vision, reduces dependence rates and increases quality of life indices (Collignon et al., 2011; Parmeggiani et al. 2011). Vision rehabilitation carried out in this context is based on the principle of stimulating repetitive synaptic activity and creating a long-term potentiation in synaptic transmission in order to activate the restoration that occurs with neuroplasticity (Schumacher et al., 2008; Essue et al., 2014).

In their experimental studies, Hooks and Chen (2020) concluded that in the development of experience-dependent neuroplasticity, spontaneous or applied experiences cause activation of the circuits in the retina and thalamus, between the thalamus and the cortex, and within the cortex itself, and changes in the connections between cortical inhibitory interneurons. They also found that experience-dependent neuroplasticity enables the restructuring of networks extending from the retina to the thalamus and cortex. Rehabilitation provides restoration of the system and the establishment of new stimulus-response relationships in the sensory system of the brain. The methods used for this are visual experience, visual training (Li 2005; Liu 2007) or non-invasive electric current stimulation of the brain (Silvestri 2021). Today, behavioral stimulation (training) of vision is by far the most common.

In diseases that cause progressive vision loss, the patient activates many sensorimotor compensation mechanisms to replace the lost ability. As vision decreases, people develop new sensorimotor strategies and visual search patterns in order to control body posture and prevent unwanted collisions (Berencsi, Ishihara, & Imanaka, 2005; Dosher, 2017). The goal of rehabilitation is to ensure that these adaptation efforts and sensorimotor compensation skills are most appropriate to the patient's needs and at the highest level. This requires a 2-step application (Jackson et al., 2022). The first step is to increase visual acuity to the highest possible values for the person. For this purpose, non-optical devices such as optical filters, light supports, or optical devices such as glasses, spectacle magnifiers, hand magnifiers, telescopic glasses and electrooptic vision aids are given to the patient as support in the evaluation of the entire "residual vision". In order to use these devices, the patient must initially receive educational support, be taught how to use the device, and even repeat this support from time to time (Marc, Jones, Watt, & Strettoi, 2003; Merabet & Pascual-Leone, 2010). The second step is the development of compensation mechanisms and this is achieved through vision perception rehabilitation. The main purpose of visual perception rehabilitation is to increase the utilization rates of residual vision, as well as to improve sensorimotor compensation by utilizing neuroplasticity and to ensure the patient's environmental adaptation (Petriçli, Merdoğan, Tunay and Özdemir, 2015; Lunghi et al., 2019; Baroncelli and Lunghi, 2022; Timlioğlu İper, İdil 2022).

Although CD is an important cause of low vision and vision loss, especially in productive ages, and rehabilitation is carried out by multidisciplinary teams in developed countries, all stages of rehabilitation cannot be completed in our country. This results in increased rates of disability and dependence in patients. However, in patients with progressive vision loss that eventually leads to vision loss, visual rehabilitation is necessary to activate brain plasticity, enable the acquisition of new skills that replace lost skills, and increase their functional vision. Providing these people with the opportunity to use their residual vision and increase their functional vision, and to develop new skills instead of the ones they have lost, will support these people to participate in social life, engage in professional production and continue their lives as autonomous individuals. In this context, the aim of this study is to increase the visual skills and functional vision of people with low vision due to HRD/Cone Dystrophy (CD) and to create a beginning for the development of vision rehabilitation approaches that reduce the level of disability and increase participation in social production. Because there are very few international studies on functional vision and its impact on quality of life and disability rates in patients with HRD, and there are no studies on this subject in our country. Reviewing low vision rehabilitation applications from an ophthalmologist's perspective and evaluating their effectiveness will contribute significantly to the creation of patient-specific rehabilitation programs and the scientific evaluation of the results. Therefore, the main hypothesis of the research is as follows:

H1: Visual rehabilitation applications increase functional vision skills, quality of life and the ability to live autonomously in hereditary retinal dystrophies.

MATERIALS AND METHODS

The research was designed as a quantitative quasi-experimental research. The research was conducted using a quasi-experimental design with a pretest-posttest comparison group. Pretest-posttest comparison group design is the measurement of participants regarding the dependent variable before and after the experimental research (Karasar, 2009). The study population of the research consists of 180 patients registered at Ankara University Ophthalmology Clinic, Low Vision Rehabilitation and Vision Research Center. In the power analysis performed, the minimum sample size was calculated as 16 patients with 80% margin of power and 5% margin of error. Since cone dystrophies are in the rare disease group, the patients' values before rehabilitation applications were used as the control group. In this context, 21 people were randomly included in the study, and 19 patients who participated in all stages of the study were included in the final evaluation. All individuals included in the study were informed about the purpose of the study, the procedures to be followed, the research protocol, the duration and risks of the study, and a written consent form was obtained.

In order to confirm the diagnoses of HRD and CD in all patients, previously taken ERGs were used, and in patients who did not have them, ERG was taken. The examinations were carried out by the researcher. ETDRS chart was used for visual acuity examination. Low vision center technicians were used to perform contrast sensitivity, microperimeter, MNRead reading test and NVFQ-25 tests. Before contrast sensitivity, MNRead and microperimeter tests were performed, all patients were given a trial session to complete the learning curve.

Near reading performance and MNRead Test: It was first developed by the University of Minnesota in 1989 to measure reading acuity, critical print size and maximum reading speed in people with low vision. The scale, which was validated in Turkish by İdil et al. (İdil, 2011) in 2011, has 19 sentences ranging from 0.5 to 1.3 logMAR values and with 0.1 logarithmic intervals. Each sentence consists of 3 lines and 60 characters. During the measurement, in addition to LogMAR values, M quantities and Snellen values are also seen. The values obtained here are collected under 4 headings. These are ACC (Reading Accesibility Index), RA (Reading Acuity), CPS (Critical Print Size) and MRS (Maximum Reading Speed).

Contrast sensitivity (CS) and testing: Contrast sensitivity (CS) is the ability to detect sharp and clear outlines of very small objects and separate them from the background. It can also be referred to as the ability to identify small differences in shadows and patterns. CS also allows us to notice objects without clear boundaries (Xiong, 2020). In the study, the Vision Monitor2016J contrast sensitivity measurement device and the "Contrast static Low vision" program within the Ankara University Low Vision Rehabilitation and Vision Research Center were used for contrast measurements.

National Eye Institute Visual Functioning Questionnaire 25 (NEI-VFQ-25) Quality of Life Scale: The quality of life scale allows people to evaluate their own health status outside of medical examination methods. NEI-VFQ 25 allows people to evaluate eleven dimensions of visual function and the effectiveness of treatment, and therefore their own visual function and perceived quality of life in different eye problems. It was validated into Turkish in 2005 by Toprak et al. It evaluates 11 visual functions: general vision, ocular pain, near activities, distant activities, visual impairment in social activities, cognitive health, role difficulties, loss of autonomy, driving, color vision, and visual field. The answers to the questions in the survey are scored between 0 and 100 according to their numerical values. These scores represent the percentage achieved of the total possible score. For example, 25 points represents 25% of the highest possible score. In the second step, items within each subscale are averaged together to create 12 subscale scores. Visual target subscale scores are averaged to calculate the total composite score for the VFQ-25. The general health question is excluded from the average. In our study, changes in both general scoring and section-based scoring were used.

Microperimetry: In our study, the MAIA (Macular Integrity Assesment) device within the Ankara University Low Vision Rehabilitation and Vision Research Center was used for microperimetry measurements. Microperimetry evaluates the morphology of the retina with the Scanning Laser Ophthalmoscope. It measures the sensitivity of the retina, that is, the minimum light intensity that the patient can detect at central 10 degrees. In an intact macula, light sensitivity should be greater than 25dB. Macular integrity is the ratio of the difference between the answers given by the patient and the answers expected in the age group. The closer it is to 0, the more normal the macular index is considered. Central fixation activity is an important finding in microperimetry, especially in macular diseases. The more fovea the patient can fixate, the higher the quality of vision. With the microperimeter, it is possible to determine the capacity to perform central fixation and the fixation point if the fixation is not fully foveal. Fixations made at a distance of 1 and 2 degrees from the foveal center, respectively, are determined as P1 and P2. P1 value indicates foveal fixation, and 75% and above is an indicator of good central fixation. BCEA: Calculates the area and orientation of an ellipse formed by fixation points. Here lower BCEA values indicate better fixation stability.

MVPT-4 (Motor free visual perceptual skills test-4): MVPT-4 was developed by Colarusso and Hammill, (2015) as the latest version of MVPT (1972), with the aim of measuring visual perception abilities independent of motor abilities in individuals. It consists of 7 sections consisting entirely of shapes, measuring five visual perception skills in a time-indexed manner. The average application time is 15 minutes and it can be applied after the age of 4. Each figure is shown for 5 seconds and the patient is asked to answer in 5 seconds. The test shows the person's average percentile and success score in each visual perception skill. The desired visual perception skill is above 90% percentile and obtaining a 9/9 result in each section.

AAO's 2022 HRD evaluation (Baroncelli and Lunghi, 2021) and low vision rehabilitation guidelines were used in planning, carrying out and evaluating the effectiveness of vision rehabilitation (Fontenot, 2018; Jackson, 2022; Silvestri, 2022). The rehabilitation program to be implemented was designed in two separate parts. The first part was general exercises and was applied manually to all patients. In designing manual programs, studies of Richman and Cron (1988), Colignon et al. (2011), Leong et al. (2014), and Elsman et al. (2019) were taken as basis.

In the second part, the Digital Optics Trainer program was used to specifically target the skills that the person wanted to develop. In organizing digital exercises, Fox and Stryker (2017) and Fortenbacher et al. (2018) applications were used. Both types of exercises were applied sequentially in each rehabilitation session. Rehabilitation applications were carried out by the technician under the supervision of the researcher and together with the researcher. Bernell Vision Trainer (Optic Trainer) was used for digital exercises. This method was chosen because it has 24 different study programs that can be chosen according to the visual skills desired to be developed, it allows the creation of different personalized programs according to visual skill scores, and the patient's scores can be followed. All manual and digital rehabilitation programs were created according to Vision Therapy Guides and studies on this subject (Reichman and Cron 1988; Leong et al., 2014; Fox and Stryker 2017; Fortenbacher et al., 2018; Sasso, 2019).

Cardinal eye movements, vergence, saccade and spatial localization marking exercises were chosen in general exercise applications. Saccades and spatial localization marking were specifically included in the study because they are defined as basic movement exercises in the development and maintenance of vision in the literature and are considered as movements that increase visual sensitivity (Sabel et al., 2011; Shütz et al., 2009; Mayeli, 2019; Sale, 2022). In the first stage of the study, the MVPT-4 test was used to determine the necessity of personalized exercises. The exercises were performed 3 days a week for 40 minutes for 2 weeks, and after the end of the exercises, visual acuity, contrast sensitivity, reading speed test, microperimeter, visual perception skills and quality of life were re-evaluated.

In our study, in addition to ophthalmological examination methods and devices, tests measuring functional vision, surveys determining quality of life and dependency rates on others, ICF coding used to evaluate disability rates was also employed.

Statistical evaluation was made with IBM SPSS 25.0 (IBM Corp., Armonk, NY, USA) package program. The conformity test for normal distribution was evaluated with the Kolmogorov-Smirnov Test. Normally distributed numerical variables were given as mean ± standard deviation, non-normally distributed numerical variables were given as median (25th - 75th percentile), and categorical variables were given as frequency (%). The difference between groups was evaluated with the Independent Sample t test for numerical variables with normal distribution. In tests of two-sided hypotheses, $p<0.05$ was considered sufficient for statistical significance.

FINDINGS

The mean age of the individuals participating in the research is 16.58±7.32. The participants consisted of 19 people in total, 9 men and 10 women.

A comparison was made between the scores of MVPT-4 Variables before and after the experiment. The post-test mean scores of DISCRIMINATION, SPATIAL LOCALIZATION and VISUALCLOSURE values are significantly higher than the pre-test mean scores ($p<0.05$). There was no significant effect of the intervention program applied on MEMORY and FIGUREGROUND values (p>0.05). The results of the analysis are shown in Table 1.

Table 1. Comparison of MVPT-4 Variables according to pre- and post-experiment scores

	Groups	N	Mean	S.S.	t	df	p
DISCRIMINATION	Pre-test	19	,6143	,10727	-3,626	36	,001*
	Post-test	19	,7662	,14775			
SPATIAL	Pre-test	19	,5615	,13107	-2,672	36	,011*
	Post-test	19	,6727	,12553			
MEMORY	Pre-test	19	,8306	,16699	-1,316	36	,196
	Post-test	19	,9006	,16103			
FIGUREGROUND	Pre-test	19	,5731	,19712	-1,128	36	,267
	Post-test	19	,6667	,30322			
VISUALCLOSURE	Pre-test	19	,6785	,18119	-2,147	36	**,039***
	Post-test	19	,7955	,15373			

A comparison was made between the pre- and post-experiment scores of MNREAD Variables. Accordingly, the post-test mean scores of max reading speed, ACC, RA were higher than the pre-test mean scores. On the other hand, the post-test mean scores of critical print size values were lower than the pre-test mean scores. However, these findings are not statistically significant (p>0.05). The results of the analysis are shown in Table 2.

Table 2. Comparison of MNREAD Variables according to pre- and post-experiment scores

	Groups	N	Mean	S.S.	t	df	p
Max. reading speed	Pre-experiment	19	71,6842	27,50364	-1,828	36	,076
	Post-experiment	19	90,2105	34,58416			
ACC	Pre-experiment	19	,3447	,13480	-1,505	36	,141

	Post-experiment	19	,4200	,17130			
RA	Pre-experiment	19	,3947	,17787	-1,118	36	,271
	Post-experiment	19	,4526	,13892			
Critical print size	Pre-experiment	19	1,4789	,71847	1,361	36	,182
	Post-experiment	19	1,2053	,50163			

CONTRAST SENSITIVITY Variables were compared according to pre- and post-experiment scores. Accordingly, the post-test mean scores of contrast sensitivity values were significantly higher than the pre-test mean scores ($p < 0.05$). The results of the analysis are shown in Table 3.

Table 3. Comparison of CONTRAST SENSITIVITY Variables according to pre- and post-experiment scores

	Groups	N	Mean	S.S.	t	df	p
0.5-1.0cpd	Pre-experiment	19	10,632	5,7851	-2,813	36	**,008***
	Post-experiment	19	15,316	4,3850			
1-2cpd	Pre-experiment	19	12,263	5,4756	-2,708	36	**,010***
	Post-experiment	19	16,684	4,5467			
2-4cpd	Pre-experiment	19	10,579	6,2389	-2,770	36	**,009***
	Post-experiment	19	15,421	4,3756			
4-5cpd	Pre-experiment	19	7,526	5,1894		36	**,012***

	Post-experiment	19	12,053	5,3174	-2,655		
5-10cpd	Pre-experiment	19	2,684	3,2669	-2,400	36	**,022***
	Post-experiment	19	5,421	3,7463			

Corrected Distance Vision, MVPT-4 and NVFQ25 Variables were compared according to their pre- and post-experiment scores. Accordingly, the post-test mean scores of MVPT-4 and NVFQ25 values were significantly higher than the pre-test mean scores ($p<0.05$). There was no statistically significant difference between the corrected distance vision mean scores ($p>0.05$). The results of the analysis are shown in Table 4.

Table 4. Comparison of Corrected Distance Vision, MVPT-4 and NVFQ25 Variables according to pre- and post-experiment scores

	Groups	N	Mean	S.S.	t	df	p
Corrected Distance Vision Right	Before Rehabilitation	19	,1726	,11194	-,367	36	,715
	After Rehabilitation	19	,1837	,06825			
After Corrected Distance Vision Rehabilitation Right	Before Rehabilitation	19	,2147	,17008	,123	36	,903
	After Rehabilitation	19	,2079	,17229			
Before MVPT-4	Before Rehabilitation	19	29,4211	4,43867	-3,516	36	**,001***
	After Rehabilitation	19	34,8421	5,04715			
Pre-NVFQ25	Before Rehabilitation	19	60,4784	14,22228	-2,617	36	**,013***

	After Rehabilitation	19	71,5668	11,78545

The before and after score means of NVFQ-25 subparameter statistics were calculated and they are shown in Table 5.

Table 5. Before and after score means of NVFQ-25 subparameter statistics

		Before Rehabilitation				**After Rehabilitation**				
	N	Min.	Max.	Mean	Std. Dev.	Min.	Max	Mean	Std. Dev.	Difference
General Health	17	25,00	100,00	55,8824	22,58562	25,00	100,00	58,8235	17,54721	2,9412
General Vision	17	,00	75,00	29,4118	20,22393	0,00	75,00	48,5294	24,15864	19,1176
Eye Pain	17	25,00	100,00	79,4118	24,58292	50,00	100,00	83,8235	18,62705	4,4118
Nearby Activity	17	29,16	87,50	60,7594	15,32331	41,60	91,60	70,0459	11,16301	9,2865
Distance Activity	17	25,00	87,50	63,2288	17,50883	41,60	91,67	69,5988	15,23175	6,3700
GS Social Function	17	33,30	100,00	71,5618	20,63672	58,30	100,00	79,8641	12,16716	8,3024
GS Mental Health	17	25,00	85,00	56,8135	17,26571	25,00	100,00	63,2335	20,19090	6,4200
GS Role Challenge	17	12,50	87,50	46,3206	20,38187	31,20	93,75	60,9971	20,87347	14,6765

GS Dependence	17	18,75	100,00	55,5118	25,37468	18,75	100,00	68,1141	25,91947	12,6024
Driving	17	,00	83,33	6,3724	20,73429	0,00	66,67	7,3512	20,80430	0,9788
Color Vision	17	,00	100,00	77,9412	30,46816	25,00	100,00	83,8235	26,42971	5,8824
Peripheral Vision	17	25,00	100,00	55,8824	24,25356	25,00	100,00	61,7647	23,58106	5,8824

MICROPERIMETRY variables were compared according to the scores of pre- and post-experiment. Accordingly, there is no statistically significant difference between the groups (p>0.05). 8 patients were able to complete the test in the first stage and these patients were included in the analysis. The results of the analysis are shown in Table 6.

Table 6. Comparison of MICROPERIMETRY variables according to pre- and post-experiment scores

	Groups	N	Mean	S.S.	t	df	p
Macular Int. RIGHT	Pre-experiment	8	92,6500	11,15437	-,992	8,914	,347
	Post-experiment	8	96,8250	4,16473			
Macular Int. LEFT	Pre-experiment	8	97,1375	4,08619	,254	14	,803
	Post-experiment	8	96,5250	5,47220			
Average Sensitivity RIGHT	Pre-experiment	8	19,5250	8,30314	-,920	14	,373
	Post-experiment	8	22,3625	2,69016			

Average Sensitivity LEFT	Pre-experiment	8	21,8750	3,89496	-,882	14	,392
	Post-experiment	8	23,2500	2,06328			
Fixation stability RIGHT P1	Pre-experiment	8	,29625	,270023	-,366	14	,720
	Post-experiment	8	,35125	,328479			
Fixation stability RIGHT P2	Pre-experiment	8	,5712	,27931	-,461	14	,652
	Post-experiment	8	,6363	,28525			
Fixation stability SOL P1	Pre-experiment	8	,2963	,31359	-,040	14	,968
	Post-experiment	8	,3025	,30499			
Fixation stability LEFT P2	Pre-experiment	8	,5325	,31590	-,313	14	,759
	Post-experiment	8	,5788	,27456			
BCEA%63 RIGHT	Pre-experiment	8	25,8375	34,63866	,722	14	,482
	Post-experiment	8	16,2375	14,70072			
BCEA%63 LEFT	Pre-experiment	8	30,6125	31,82557	,860	14	,404
	Post-experiment	8	19,8000	15,85299			
BCEA%95 RIGHT	Pre-experiment	8	77,4250	103,85639	,722	14	,482

	Post-experiment	8	48,6500	44,01191			
BCEA%95 LEFT	Pre-experiment	8	91,8000	95,43143	,860	14	,404
	Post-experiment	8	59,3625	47,55472			

ICF codes of the participants were determined and these codes are presented in

Table 7.codes of the particZipants

Participant	b140	b210	b2100	b2102	b2152	d220	d315	d335	d420
P1	2	2	2	2	3	2	3	0	3
P2	0	3	3	3	2	0	2	1	1
P3	0	3	3	2	3	1	2	2	2
P4	2	3	3	2	3	2	3	0	2
P5	1	3	3	3	0	3	3	3	2
P6	1	3	3	3	0	1	3	0	3
P7	0	3	3	3	0	2	3	3	2
P8	1	3	3	2	3	0	3	0	3
P9	1	3	3	3	3	0	3	3	2
P10	0	3	3	2	0	1	3	1	2
P11	1	3	3	3	3	2	2	2	3
P12	2	3	3	3	0	1	3	2	2
P13	1	3	3	3	3	1	2	1	2
P14	0	3	3	1	3	1	2	0	2
P15	1	3	3	1	0	1	3	2	2
P16	2	2	2	2	0	2	2	0	3

P17	0	3	3	3	0	1	2	2	2
P18	1	3	3	2	3	1	2	2	3
P19	0	3	2	2	0	0	2	2	3

NOTE: b140: attention; b210: visual function; b2100: binocular vision, b2102: quality of vision, b2152: nystagmus, d220: multitasking, d315: understanding non-verbal messages, d335: producing non-verbal messages, d420: self-displacement, d720: complex interpersonal interactions.

DISCUSSION AND CONCLUSION

Inherited retinal disorders are among the most complex genetic diseases in the world, requiring a wide range of genetic tests and treatments. Since they affect vision, especially from early childhood, they prevent the child from completing the developmental stages that he can complete with visual guidance and limit people's ability to participate in social production and individual living. Studies conducted in these patients are mostly related to Retinitis pigmentosa (RP) (Begenisic et al., 2020; Lungi et al., 2019). Lungi and Berenisic showed that there is a significant cortical neuroplasticity in RP patients and that this can be maintained until the advanced stages of RP. No studies on neuroplasticity in cone dystrophies have been found in the literature. In this context, the present research has a high original value. The main purpose of our study is to investigate the existence of neuroplasticity and the level of benefit from visual rehabilitation treatment in order to give CD patients, who are far from social efficiency and autonomy, the skills to participate in production and live more autonomously. The aim is not to increase visual acuity, but to increase visual functions and functional vision by utilizing residual vision and neuroplasticity.

Li et al. (2005) and Liu et al. (2007) showed that perceptual learning exercises increased contrast sensitivity and increased visual skills such as visual search and reading speed in children with low vision. Aslan and Çakmak (2016) were able to increase the monitoring skills of children with low vision with functional vision exercises. It was shown that the skills developed through perceptual learning led to the development of different visual skills beyond the skills that the training focuses on, just like in visually unimpaired individuals (Nyquist et al., 2016). Bier and Fröhlich (2009) and Begenisic et al. (2020) investigated patients with hereditary retinal dystrophies and especially retinitis pigmentosa. They found in their study that despite the progressive loss of retinal photoreceptors in RP, the visual cortex maintains a remarkable ability to input-dependent remodeling, that is, neuroplasticity is also preserved in these patients. This indicates that the quality of life can be improved in HRD patients.

The results we obtained in our study support the view that the activity of neurons that are provided with rich visual experience will be high, thus sending more intense stimulation to the cortex, which will lead to the strengthening of snaps (Baroncelli and Lunghi, 2021). In addition, these results are also compatible with the study of Peli et al. (2016), who stated that people with low vision developed new fixation and saccade models to increase their environmental awareness. In this study, patients were shown which saccade and fixation models they could use, apart from the spontaneous movements developed by the patient. In our study group, visual perception skills were monitored with the MVPT-4 test, and the percentage rates were found to be low according to age in all stages of the test before rehabilitation. In the subgroups of the test, it was observed that discrimination, spatial localization, figure-ground perception and visual memory skills constituted the lowest group. The patients were given manual and digital discrimination, saccade, and spatial localization exercises. In the repeated test after rehabilitation, it was observed that the total test success increased and there was a statistically significant increase in discrimination, spatial localization and visual closure skills.

Saccadic ability is essential not only for the physical act of reading, but also for the cognitive and visual attention processes that underlie reading proficiency. Therefore, saccadic movement rehabilitations have an effect on visual perception and visual sensitivity (Leong et al., 2014). In our study, a significant increase in reading speed and a decrease in critical print size were detected in reading speed measurements made with the MN-Read test. This result is also compatible with Leong et al.'s (2014) study showing the enhancing effect of saccadic exercises on reading performance.

In our study, an increase in contrast sensitivity values was observed in all patients, especially at low frequency and high contrast values. This finding is compatible with the studies of Schütz (2009) and Mayeli (2019), who reported the positive effect of saccadic eye movements and perceptual rehabilitation on contrast sensitivity values. Studies have shown that stimulation of the parvocellular retinogeniculate pathway by smooth pursuit movements of visual sensitivity leads to increased contrast gain. Zaidi et al. (2014) showed in their study that transient neuronal responses caused by eye movements contribute to edge awareness and brightness perception. Casile et al. (2019), Giari et al., (2023) and Nau et al. (2018) stated that the enterorhinal cortex and hippocampal formation (HF) mediate the visual representation of the outside world through several basic neural mechanisms, and these mechanisms include place cells, grid cells, border cells, head direction (HD) cells, spatial localization cells, contrast sensitivity cells, visual border cells, and visual saccade direction (SD) cells. These cells encode a world-centered map of the visual field and the direction of eye movements, allowing the brain to reconstruct its own movement and maintain stable world-centered representations of the visual field during movements. These studies also explain the increased spatial localization and visual closure skills in our patients. Visual closure is the ability to perceive the entire object or scene, part of which is seen. For example, understanding that a shape with one end visible belongs to a table is visual closure. In our study, the increase in contrast sensitivity as well as the increase in visual perception skills such as discrimination and visual closure were thought to be compatible with the mechanisms in these studies.

Brown (2012) showed in his study that an increase in visual perceptual skills also causes an increase in visuomotor skills. The hippocampal formation also plays an important role in the context of navigation and memory, shaping our visual experience and supporting cognitive operations related to visual exploration and perception. Vision-derived information flow from spatial experiences also causes an increase in spatial skills in patients (Nau et al., 2018). In our study, 2 different manual exercises were applied for spatial rehabilitation. It is one of the skills that showed the most significant increase in all patients. Our findings are consistent with the studies of Brown and Nau.

Van Nispen et al. (2020) showed in their study in adults that multidisciplinary low vision rehabilitation helps individuals adapt to vision loss, improve their psychosocial well-being and improve their ability to perform daily activities, ultimately improving their quality of life. In our study, it was observed that patients with CD experienced the most problems in role difficulty, individual autonomy, and nonverbal communication. They expressed an increase in quality of life in these areas after rehabilitation. After visual perception rehabilitation, significant improvements were observed in the quality of life index, role difficulty and independence parameters. This positive effect is thought to be a result of the development of people's spatial evaluation skills.

De Carlo (2015) showed in his study that nystagmus has effects such as decrease in visual skills and low vision, as well as lack of self-confidence, decrease in quality of life and increase in dependence rates. In our study, 11 out of 19 patients were unable to complete the microperimetry test before rehabilitation, and only 8 patients were able to perform the test. Of the 11 patients who could not complete the test after rehabilitation applications, 5 more were able to complete the test. Although this finding could not be compared due to the fact that there was no study on microperimetry in HRD/Cone dystrophies in the literature, it is one of the most important findings of the study. Studies stating that the frequency of nystagmus decreases and fixation increases in cases where the foveal residence time of the image can be extended or brought closer to the fovea in nystagmus (Penicks, 2015; Leung, 1996) suggested that our finding may have been affected by vergence and discrimination studies.

As a result, the current study revealed that the quality of life in HRD/CD patients is significantly affected and the most important factors that impair their quality of life are role difficulty and loss of individual autonomy. On the other hand, it was determined that visual abilities of 33% can be increased to 46% and above with short-term neuroplasticity. The continuity of this increase and the level at which it can increase with long-term studies indicate the need for further studies on this subject. Moreover, it was determined that even in cases where visual acuity cannot be increased, improvements can be achieved in other elements of functional vision. Here, an increase was reported in contrast sensitivity levels, reading speed and visual perception levels. In the research, discrimination, spatial localization and visual closure skills came to the fore among the areas where the increase in visual perception level was highest. Therefore, an increase in satisfaction and quality of life was observed in the elements of role difficulty and independence. The 6-hour rehabilitation was not sufficient to change the patients' ICF codes. However, quality of life and visual skills was shown to improve. Although there is insufficient time for the development of long-term neuroplasticity, the rapid and positive responses showed that neuroplasticity is preserved in hereditary diseases and that rehabilitation applications increase visual skills and functional vision.

REFERENCES

1. Aslan, C., & Çakmak, S. (2016). İşlevsel görme aktivite programı ile az gören çocuğun izleme becerilerinin geliştirilmesi. Ankara Üniversitesi Eğitim Bilimleri Fakültesi Özel Eğitim Dergisi, 17(01), 59-77 https://doi.org/10.1501/Ozlegt_0000000239
2. Baroncelli, L., & Lunghi, C. (2021). Neuroplasticity of the visual cortex: in sickness and in health. Experimental neurology, 335, 113515. DOI: 10.1016/j.expneurol.2020.113515
3. Begenisic, T., Mazziotti, R., Sagona, G., Lupori, L., Sale, A., Galli, L., & Baroncelli, L. (2020). Preservation of visual cortex plasticity in retinitis pigmentosa. Neuroscience, 424, 205-210. DOI: 10.1016/j.neuroscience.2019.10.045
4. Berardi, N., Sale, A., & Maffei, L. (2015). Brain structural and functional development: genetics and experience. Developmental Medicine & Child Neurology, 57, 4-9. DOI: 10.1111/dmcn.12691
5. Berencsi, A., Ishihara, M., & Imanaka, K. (2005). The functional role of central and peripheral vision in the control of posture. Human movement science, 24(5-6), 689-709. DOI: 10.1016/j.humov.2005.10.014
6. Bier, C. M., & Fröhlich, S. J. (2009). Visual rehabilitation in patients with hereditary retinal dystrophy: current data from a low vision department. Klinische Monatsblatter fur Augenheilkunde, 226(5), 421-427. DOI: 10.1055/s-0028-1109264
7. Birtel, J., Eisenberger, T., Gliem, M., Müller, P. L., Herrmann, P., Betz, C., & Charbel Issa, P. (2018). Clinical and genetic characteristics of 251 consecutive patients with macular and cone/cone-rod dystrophy. Scientific Reports, 8(1), 4824. DOI: 10.1038/s41598-018-22096-0
8. Brown, T. (2012). Are motor-free visual perception skill constructs predictive of visual-motor integration skill constructs? Hong Kong Journal of Occupational Therapy, 22(2), 48-59. https://doi.org/10.1016/j.hkjot.2012.06.003
9. Burton, M. J., Ramke, J., Marques, A. P., Bourne, R. R. A., Congdon, N., Jones, I., ... & Faal, H. B. (2021). The Lancet Global Health Commission on Global Eye Health: vision beyond 2020. Lancet Glob Health. 9(1), 489-551. DOI: 10.1016/S2214-109X(20)30488-5
10. Casile, A., Victor, J. D., & Rucci, M. (2019). Contrast sensitivity reveals an oculomotor strategy for temporally encoding space. Elife, 8, 409-424. https://doi.org/10.7554/eLife.40924
11. Colarusso, R., & Hammill, D. (2015). Motor-Free Visual Perception Test-4 (MVPT-4) (4th ed.). Novata, CA: Academic Therapy Publications
12. Collignon, O., Champoux, F., Voss, P., & Lepore, F. (2011). Sensory rehabilitation in the plastic brain. Progress in brain research, 191, 211-231. DOI: 10.1016/B978-0-444-53752-2.00003-5

13. Elsman, E. B., Al Baaj, M., van Rens, G. H., Sijbrandi, W., van den Broek, E. G., van der Aa, H. P., ... & van Nispen, R. M. (2019). Interventions to improve functioning, participation, and quality of life in children with visual impairment: a systematic review. Survey Of Ophthalmology, 64(4), 512-557. https://doi.org/10.1016/j.survophthal.2019.01.010
14. Essue, B. M., Li, Q., Hackett, M. L., Keay, L., Iezzi, B., Tran, K. D., ... & VISIONARY Study Team. (2014). A multicenter prospective cohort study of quality of life and economic outcomes after cataract surgery in Vietnam: the VISIONARY study. *Ophthalmology*, *121*(11), 2138-2146.
15. Fontenot, J. L., Bona, M. D., Kaleem, M. A., McLaughlin, W. M., Morse, A. R., Schwartz, T. L., ... & Jackson, M. L. (2018). Vision rehabilitation preferred practice pattern®. Ophthalmology, 125(1), P228-P278. DOI: 10.1016/j.ophtha.2017.09.030
16. Fortenbacher, D. L., Bartolini, A., Dornbos, B., & Tran, T. (2018). Vision therapy and virtual reality applications. Advances in Ophthalmology and Optometry, 3(1), 39-59. DOI: 10.1016/j.yaoo.2018.04.002
17. Fox, K., & Stryker, M. (2017). Integrating Hebbian and homeostatic plasticity: introduction. Philosophical Transactions of the Royal Society B: Biological Sciences, 372(1), 201-213. DOI: 10.1098/rstb.2016.0413
18. Georgiou, M., & Michaelides, M. (2021). Progressive and Stationary Disorders of Cone Function: Cone and Cone-Rod Dystrophies and Cone Dysfunction Syndromes. In Albert and Jakobiec's Principles and Practice of Ophthalmology (pp. 1-29). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-42634-7_2
19. Giari, G., Vignali, L., Xu, Y., & Bottini, R. (2023). MEG frequency tagging reveals a grid-like code during attentional movements. Cell Reports, 42(10). https://doi.org/10.1016/j.celrep.2023.113209
20. Gill, J. S., Georgiou, M., Kalitzeos, A., Moore, A. T., & Michaelides, M. (2019). Progressive cone and cone-rod dystrophies: Clinical features, molecular genetics and prospects for therapy. British Journal of Ophthalmology, 103(5), 711–720. https://doi.org/10.1136/bjophthalmol-2018-313278
21. Hooks, B. M., & Chen, C. (2020). Circuitry underlying experience-dependent plasticity in the mouse visual system. Neuron, 106(1), 21-36. DOI: 10.1016/j.neuron.2020.01.031
22. Idil, A. (2011). Az gören çocuklarda görsel rehabilitasyon. Turkiye Klinikleri J Ophthalm-Special Topics, 4, 73-78. DOI: 10.4274/tjo.82653
23. Jackson, M. L., Virgili, G., Shepherd, J. D., Di Nome, M. A., Fletcher, D. C., Kaleem, M. A., ... & Riddering, A. T. (2022). Vision rehabilitation preferred practice pattern. Ophthalmology, 20(1), 161-164. DOI: 10.1016/j.ophtha.2022.10.033
24. Karasar, N. (2009). Bilimsel Araştırma Yöntemleri. Ankara: Nobel Yayınları
25. Leong, D. F., Master, C. L., Messner, L. V., Pang, Y., Smith, C., & Starling, A. J. (2014). The effect of saccadic training on early reading fluency. Clinical pediatrics, 53(9), 858-864. DOI: 10.1177/0009922814532520

26. Leung, V., Wick, B., & Bedell, H. E. (1996). Multifaceted treatment of congenital nystagmus: a report of 6 cases. *Optometry and vision science*, *73*(2), 114-124.
27. Li, R. W., Young, K. G., Hoenig, P. & Levi, D. M. (2005). Perceptual learning improves visual performance in juvenile amblyopia. Invest. Ophthalmol. Vis. Sci. 46, 3161–3168 doi:https://doi.org/10.1167/iovs.05-0286
28. Liu, L., Kuyk, T. & Fuhr, P. (2007).Visual search training in subjects with severe to profound low vision. Vision Res. 47, 2627–2636 https://doi.org/10.1016/j.visres.2007.07.001
29. Lunghi, C., Galli-Resta, L., Binda, P., Cicchini, G. M., Placidi, G., Falsini, B., & Morrone, M. C. (2019). Visual cortical plasticity in retinitis pigmentosa. Investigative ophthalmology & visual science, 60(7), 2753-2763. doi: 10.1167/iovs.18-25750
30. Marc, R. E., Jones, B. W., Watt, C. B., & Strettoi, E. (2003). Neural remodeling in retinal degeneration. Progress in retinal and eye research, 22(5), 607-655. DOI: 10.1016/s1350-9462(03)00039-9
31. Mayeli, M. (2019). Neurophysiology of visual perception. Biophysics and neurophysiology of the sixth sense, 13-26. https://doi.org/10.1038/nrn2758
32. Merabet, L. B., & Pascual-Leone, A. (2010). Neural reorganization following sensory loss: the opportunity of change. Nature Reviews Neuroscience, 11(1), 44-52. https://doi.org/10.1038/ nrn2758
33. Murray, C. J., Lopez, A. D., Mathers, C. D., & Stein, C. (2001). The Global Burden of Disease 2000 project: aims, methods and data sources. Geneva: World Health Organization, 36, 1-57 https://www.ncbi.nlm.nih.gov/books/NBK11808
34. Nau, M., Julian, J. B., & Doeller, C. F. (2018). How the brain’s navigation system shapes our visual experience. Trends in cognitive sciences, 22(9), 810-825. DOI: 10.1016/j.tics.2018.06.008
35. Nyquist, J. B., Lappin, J. S., Zhang, R., & Tadin, D. (2016). Perceptual training yields rapid improvements in visually impaired youth. Scientific reports, 6(1), 37431. https://doi.org/10.1038/srep37431
36. Parmeggiani, F., Sato, G., De Nadai, K., R Romano, M., Binotto, A., & Costagliola, C. (2011). Clinical and rehabilitative management of retinitis pigmentosa: up-to-date. Current Genomics, 12(4), 250-259 DOI: 10.2174/138920211795860125
37. Peli, E., Apfelbaum, H., Berson, E. L., & Goldstein, R. B. (2016). The risk of pedestrian collisions with peripheral visual field loss. Journal of Vision, 16(15), 5-5. DOI: 10.1167/16.15.5
38. Penix, K., Swanson, M. W., & DeCarlo, D. K. (2015). Nystagmus in pediatric patients: interventions and patient-focused perspectives. *Clinical ophthalmology*, 1527-1536.
39. Petriçli, İ. S., Merdoğan, A. İ., Tunay, Z. Ö., & Özdemir, Ö. (2015). Herediter retina distrofili olgularda az görme rehabilitasyonu. Turk Oftalmoloiji Dergisi, 45(1), 25–30. https://doi.org/10.4274/tjo.22590
40. Richman, J. E., & Cron, M. T. (1988). Guide to vision therapy. Bernell.

41. Sabel, B. A., Henrich-Noack, P., Fedorov, A., & Gall, C. (2011). Vision restoration after brain and retina damage: the "residual vision activation theory". Progress in Brain Research, 192, 199-262. DOI: 10.1016/B978-0-444-53355-5.00013-0
42. Sale, A. (2022). Molecular mechanisms of neural plasticity: from basic research to ımplications for visual functional rescue. International Journal of Molecular Sciences, 23(21), 13-18. https://doi.org/10.3390/ijms232113183
43. Sasso, P., Silvestri, V., Sulfaro, M., Scupola, A., Fasciani, R., & Amore, F. (2019). Perceptual learning in patients with Stargardt disease. *Canadian Journal of Ophthalmology*, *54*(6), 708-716. https://doi.org/10.1016/j.jcjo.2019.03.012
44. Schumacher, E. H., Jacko, J. A., Primo, S. A., Main, K. L., Moloney, K. P., Kinzel, E. N., & Ginn, J. (2008). Reorganization of visual processing is related to eccentric viewing in patients with macular degeneration. Restorative neurology and neuroscience, 26(4-5), 391-402. PMID: 18997314
45. Schütz, A. C., Braun, D. I., & Gegenfurtner, K. R. (2009). Improved visual sensitivity during smooth pursuit eye movements: Temporal and spatial characteristics. *Visual neuroscience*, *26*(3), 329-340.
46. Silvestri, V., Turco, S., Piscopo, P., Guidobaldi, M., Perna, F., Sulfaro, M., & Amore, F. (2021). Biofeedback stimulation in the visually impaired: a systematic review of literature. Ophthalmic and Physiological Optics, 41(2), 342-364. DOI: 10.1111/opo.12787
47. Timlioğlu İper HS, İdil ŞA.(2022) Pediatrik olgularda görsel rehabilitasyon ve habilitasyonda güncel yötemler. Karakaş N, editör. Pediatrik Göz Hastalıkları. 1. Baskı. Ankara: Türkiye Klinikleri; p.7-13.
48. Toprak, A. B., Eser, E., Guler, C., Baser, F. E., & Mayali, H. (2005). Cross-validation of the Turkish version of the 25-item national eye institute visual functioning questionnaire (NEI-VFQ 25). Ophthalmic Epidemiology, 12(4), 259-269 DOI: 10.1080/09286580590967763
49. Van Nispen, R. M., Virgili, G., Hoeben, M., Langelaan, M., Klevering, J., Keunen, J. E., & van Rens, G. H. (2020). Low vision rehabilitation for better quality of life in visually impaired adults. Cochrane Database of Systematic Reviews, (1). DOI: 10.1002/14651858.CD006543.pub2
50. Xiong, Y. Z., Kwon, M., Bittner, A. K., Virgili, G., Giacomelli, G., & Legge, G. E. (2020). Relationship between acuity and contrast sensitivity: differences due to eye disease. Investigative Ophthalmology & Visual Science, 61(6), 40-40. doi: 10.1167/iovs.61.6.40
51. Yu, H. G. (Ed.). (2022). Inherited Retinal Disease. Springer Nature.
52. Zaidi, Q., Ennis, R., Cao, D., & Lee, B. (2014). Eye-movements and the neural basis of context effects on temporal sensitivity. Journal of Vision, 14(10), 201-201. doi: 10.1523/JNEUROSCI.1048-14.2014