RESEARCH ARTICLE

Evaluation of the ganglion cell layer thickness in children with attention deficit hyperactivity disorder and comorbid oppositional defiant disorder

Gangliyon hücre tabakası kalınlığının dikkat eksikliği hiperaktivite bozukluğu ve komorbid karşıt olma karşı gelme bozukluğu olan çocuklarda değerlendirilmesi

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SUMMARY

Object: We aimed to compare the Retinal Nerve Fiber Layer (RNFL), ganglion cell layer (GCL), and the optic nerve thicknesses (ONT) of children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) to a healthy control group; and the possible worse effect of the Oppositional Defiant Disorder (ODD).**Methods:** 31 patients, (n=16 ADHD and n=15 ADHD+ODD) and a control group of 31 participants included. The Conners' Teachers Rating Scale and the Conners' Parent Rating Scale were used for the severity of the symptoms in children. Ophthalmologic measurements performed with optic coherence tomography device. **Results:** In this study, different ophthalmologic measurements (RNFL, GCL and optic nerve thicknesses) are compared between ADHD children and controls. Results show primarily bilateral thinner GCL in ADHD children compared to controls, which is the first demonstration. Optic nerve thicknesses of right eye inferior quadrant and left eye superior quadrant, as well as mean optic nerve thickness of left eye, and furthermore both eyes total GCL thickness measurement averages with also their thicknesses in superior, inferior area of patient group were found as statistically lower ($p < 0,05$) than control group. The measured thinning of RNFL wasn't statistically significant for both eyes in patient group. **Discussion:** In patients diagnosed with ADHD, thinning of the GCL and optical nerve thicknesses were found statistically significant compared to the control group, whereas the thinning of RNFL was only numerical. ODD comorbidity was thought to have no additional effect on thinning. This may lead to the idea that the negative effect of the ODD on the neurodegenerative process may be assessed with larger sample studies.

Key Words: Retinal Nerve Fiber Layer, ganglion cell layer, optic nerve thicknesses, Attention Deficit Hyperactivity Disorder

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ÖZET

Amaç: Dikkat Eksikliği Hiperaktivite Bozukluğu (DEHB) tanısı konmuş çocukların retina sinir lifi tabakası (RSLT), ganglion hücre tabakası (GHT) ve optik sinir kalınlıklarının sağlıklı kontrol grubuyla karşılaştırılması ve karşı olma karşıt gelme bozukluğunun (KOKGB) olası olumsuz etkilerinin değerlendirilmesi amaçlanmıştır **Yöntem:**31 hasta (n = 16 DEHB ve n = 15 DEHB + KOKGB) ve 31 kişilik kontrol grubu dahil edildi. Çocuklarda semptomların şiddetini değerlendirmek için Conners Öğretmenleri Derecelendirme Ölçeği ve Conners Ebeveyn Derecelendirme Ölçeği kullanılmıştır. Optik koherens tomografi cihazı ile yapılan oftalmolojik ölçümler değerlendirilmiştir. Bu çalışmada, DEHB çocuk ve kontrolleri arasında farklı oftalmolojik ölçümler (RSLT, GHT ve optik sinir kalınlıkları) karşılaştırıldı. **Bulgular:** Elde edilen sonuçlar öncelikle DEHB olan olgularda kontrollere göre bilateral daha ince GHT'yi göstermektedir. Sağ göz inferior kadran ve sol gözde superior kadranın optik sinir kalınlıkları ile sol gözün ortalama optik sinir kalınlığı ve her iki gözün GHT kalınlık ortalamaları gözün üst ve alt bölgelerinde hasta grubuyla sağlıklı kontroller arasında istatistiksel olarak anlamlı değişiklik olduğu bulundu ($p < 0,05$). RSLT'nin ölçülen incelmesi, hasta grubunda her iki göz içinde istatistiksel olarak anlamlı değildi. **Sonuç:** DEHB tanısı alan hastalarda GHT ve optik sinir kalınlıklarının incelmesi kontrol grubuna göre istatistiksel olarak anlamlı bulunurken, RSLT'nin incelmesi sadece sayısal bir farklılık bulundu. KOKGB komorbiditesinin incelme üzerine ek bir etkisi olmadığı düşünülmedi. Bu durum KOKGB'nin nörodejeneratif sürece olumsuz etkisinin daha geniş örneklemli çalışmalarla değerlendirilmesi fikrini gündeme getirebilir.

Anahtar Sözcükler: Retinal Sinir Lif Katmanı, ganglion hücre tabakası, optik sinir kalınlık, Dikkat Eksikliği Hiperaktivite Bozukluğu

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INTRODUCTION

Attention Deficit Hyperactivity Disorder is a neuro-developmental disorder which begins in early childhood, and continues throughout the young adulthood with a ratio of 50-70% (1). ADHD affects 5% of the children population in worldwide (2). ADHD is associated with difficulties experienced in many social, academic, cognitive and emotional areas of performance(3, 4). It manifests itself in three main group of symptoms in the individual as: lack of attention, hyperactivity, and impulsiveness(1). All three groups of symptoms coexist in patients with ADHD-combined type which is the most commonly observed subtype in both genders (5). Moreover, cases those co-morbidities are present, the symptoms intensity thus adding extra burdens to social life. It has been reported that ODD accompanying ADHD with a rate of 40-80%(6).

In neuroimaging studies of the brain, it has been reported that there are neuroanatomic and functional differences in ADHD diagnosed patients compared to the normal population. Even though the formation time, specific zone and the characteristics of these morphological changes have not yet been specified, ADHD has been referred to as a neurodevelopmental disorder today (7,8).Studies about neurodevelopmental disorders have been going on for many years by studying the retinal layer that is the important reflection of the brain that we can see from the outside.

Studies investigating the visual functions and the ocular characteristics of children diagnosed with ADHD have detected significant anomalies with a high rate as; subnormal visual activity, strabismus, lessening of stereo imaging, refractive defects, contracted optical disc and rim areas, cognitive visual problems(9, 10). Cognitive functions, with their complex structure and the important role they bear in daily life; comprise a large division of the central nervous system (11). Optic nerve and retina, being differentiated from diencephalon during the embryonic development process, has been considered as part of the central nervous system (12). Furthermore, ganglion cell layer (GCL) is the final and the most integrated retinal center before the visual data is transferred to the brain (13). Retinal involvement in cognitive functions of the patients with ADHD have been supported by; retinal ganglion cell loss established in histopathological studies and decrease in retinal nerve layer thickness established in in-vivo studies (14, 15). For this reason, we can get more different ideas about whether there is a problem in the neurodevelopmental process by looking at GCL. In addition, since it is a differentiating layer from the diencephalic neurodevelopmental process, we think that it can be evaluated as a parameter that can give clues about neuronal migration.

It is beyond doubt that the diagnosis and treatment of these ocular pathologies in children with ADHD would contribute to their quality of life. Hence, we aimed to compare the retinal nerve fiber layer (RNFL), GCL and optic nerve thicknesses (ONT) of children diagnosed with ADHD with a healthy control group; and to determine possible correlations of ADHD symptoms with the ocular thickness measurements; and also, to detect contingent effects of ODD comorbidity as an aggravating factor on the basis of quantitative parameters of relevant ocular measurements.

METHODS

Sample

This study was performed with the Selcuk University non-interventional clinical researches ethics committee approval date 24.05.2017 and number 2017/10 in Aksaray University Faculty of Medicine, Department of Child and Adolescent Psychiatry and Department of Ophthalmology between January 2017-May 2017. The study included 31 children aged between 6-12 years old who were either newly diagnosed with Attention Deficit Hyperactivity Disorder or Attention Deficit Hyperactivity Disorder co-morbid Oppositional Defiant disorders (16 ADHD, 15 ADHD+ODD) according to DSM-IV-TR diagnostic criteria. A matched (by gender, age) healthy control group (n=31) without any psychiatric or ophthalmologic disorders were included to our study. Individuals with normal intelligence were included in this study. The WISC-R test and the Kent-Porteus test

(>85 score of normal intelligence) were used to assess cognitive development. When the intelligence skills were examined with the appropriate materials, those who were at the normal limit of intelligence and those who were not meet the DSM-5 learning disabilities diagnostic criteria were included in the study. Children were enrolled in the study after obtainment of written informed consent from their family.

Structured interview, K-SADS-PL (Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version) was used for diagnosis. Psychotic disorder, bipolar disorder, mental retardation, autism spectrum disorders, anxiety disorders, depression, substance abuse, severe medical/neurological diseases and learning disabilities are determined as exclusion criteria. For exclusion, K-SADS-PL and physical examination was used. Additionally, participants who were unable to comply with the eye measurement device and cases who did not volunteer to participate were excluded from the study.

Ophthalmologic measurements performed with optic coherence tomography device (OptoVue, Fremont, CA, USA). In patients with an appropriate reliability criterion of fixation; the RNFL, GCL, and the optic nerve thickness measurements in both eyes with also their thickness changes within superior (sup), inferior (inf), temporal (tem), nasal (nas) areas were recorded and evaluated.

Measures

Socio-demographic questionnaire: Includes socio-demographic data such as age, gender, educational state, socio-economical level (with Hollingshead-Redich scale) and place of residence as well as information including educational state of parents, medical history and family type. Hollingshead and Redlich Scale is a widely used system that computes SES based upon parental occupation and educational levels (years of education and educational degree earned). Lower parental SES scores indicate higher socioeconomic position.

Conner's Parents Rating Scale- Revised/Long Form (CPRS-R/L): CPRS-R/L is consisted subscales of cognitive problems/inattention, oppositionality, hyperactivity, anxiety-shyness, perfectionism, social problems and psychosomatic. DSM-IV index, ADHD index and Global Index according to DSM-IV diagnostic criteria are used for contribution. Parents are requested to answer items while taking the last one month into consideration. Each item is answered as one the following 4 choices: Not true at all (rarely), somewhat true (sometimes), quite true (mostly), completely true (almost always)(16)

Conner's Teachers Rating Scale-Revised/Long Form (CTRS-R/L): CTRS-R/L includes 38 items, six subscales and additionally three assistant scales based on the ADHD symptoms in DSM-IV: ADHD index, Conner's Global Index and DSM-IV Symptoms Index. Teachers are requested to evaluate children/adolescent's behaviors while taking the last one month into consideration. For each item 4 answer choices represented as mention above (17)

Wechsler Intelligence Scale for Children (WISC-R): The test which had been devised in 1949 by Wechsler has been revised in 1974 and standardized for use in our country in 1995 by Savasır and Sahin. WISC-R comprises of two sections which are 'verbal' and 'performance'. Each section contains 6 subtests. For the verbal section: Comprehension, Similarities, Arithmetic, Reasoning, Number Sequences; and for the performance section: Picture Completion, Picture Design, Block Design, Assembling, and Cypher Decoding have been utilized. Test reliability results have been established as 0.97 for the Verbal Section, 0.97 for Performance Section, and 0.97 for the total score as the quotient (18).

Kent-Porteus Test: Developed by Kent and Grace H. in 1941. It is a paper pen test based on verbal performance applied to children over 6 years of age. It can be applied to patients and healthy people who do not have hearing and speech problems. The total IQ score is obtained by summing the sub-test scores. It is used to help the clinician support his opinion about intelligence.

Statistical analysis

All data were analyzed with SPSS (Statistical

Package for the Social Sciences) software for Windows (v21.0; IBM, Armonk, NY, USA). Individual and aggregate data were summarized using descriptive statistics including mean, standard deviations, medians (min-max), frequency distributions and percentages. Evaluation of categorical variables performed by Chi-Square test. Comparison of the variables with normal distribution was made with Student t test and ANOVA (Post Hoc Tukey analysis in multiple groups comparisons). For the continuous variables that were not normally distributed, the Mann Whitney test was conducted to compare between groups. Presence of correlation was analyzed with Spearman's Rho and Pearson tests. P-values of <0.05 were considered statistically significant.

RESULTS

Of the 62 participants included in the study, 16 were diagnosed with ADHD, 15 were diagnosed ADHD+ODD, and 31 were healthy control group. A total mean age of the ADHD group was 111,62± 27.05 months, ADHD+ ODD group was 114,46± 28,33 months, and the control group was 127,19 ± 24,39 months (Table 1). Sociodemographic data were compared between groups with appropriate compare means test according to whether data is distributed normal or not. No statistically significant differences found between the groups according to age and gender (p> 0,05).

16 of the participants (25,8%) have been applied the WISC-R test (Verbal Intelligence Points Average=93,93±11.05, Performance Intelligence Points Average= 93,18±10,14); and the remaining 46 (74,2%) were applied Kent-Porteus Test (Average Points = 96,47±8.6). In addition, comparisons of all subscale points of Conners' Parent and Teacher Rating Scales are presented in Table 2. One of the two tests, Kent-Porteus Test and WISC-R was used for evaluate intelligence taking into consideration the time and working conditions in when the patient was assessed

In our study the GCL thickness of total (right eye: 100.84±5.2 μm, left eye: 100.87±5.2 μm) superior (right eye: 100.15±5.5 μm left eye: 100.89±5.3 μm,), and inferior fields (right eye:101.56±5.3 μm left eye: 100.86±5.4 μm,) of control group have found as statistically higher than the measured total, superior and inferior GCL thicknesses in the left and right eyes of the patient group (Total Right Eye: 96.31±2.7 Total Left Eye: 97.28±3.2 Superior Right Eye: 95.79±2.9 μm Superior Left Eye: 97.09±3.5 μm Inferior Right Eye: 96.89±2.9 μm Inferior Left Eye: 97.61±3.2 μm) (p-values= 0.000-0.002, 0.000-0.002, 0.000-0.006, respectively).

Table 1. Distribution of sample group according to age and gender.

	Gender	N (%)	Age Mean±Std	P-value
Control	Female	18 (%29)	122,94±23,05	
	Male	13 (%21)	133,07±25,87	
	Total	31 (%50)	127,19±24,39	
ADHD	Female	3 (%4,8)	112,00±9,53	0,105[a]
	Male	13 (%21)	111,53±29,99	
	Total	16 (%25,8)	111,62±27,05	
ADHD+ODD	Male	15 (%24,2)	114,46±28,33	
	Total	15 (%24,2)	114,46±28,33	
Total	Female	21 (%33,9)	121,38±21,82	
	Male	41 (%66,1)	119,43±29,01	0,769[b]
	Total	62 (%100)	120,09±26,62	

a=P-value analysed among control, ADHD and ADHD+ODD groups for mean age (ANOVA Test).
b= P-value analysed between all male and female participants for mean age (Independent Samples T-Test).
ADHD: Attention Deficit Hyperactivity Disorder
ODD: Oppositional Defiant Disorder

Furthermore, it has been established that the statistically significant thinning compared to the control group, detected during the measurements of the superior, inferior and total GCL thicknesses in the left and right eye subsist when ADHD and ADHD+ODD groups are evaluated separately (p<0,05) (Table 3).

In our study detected thinning in the RNFL thickness of the left eyes of the patient group in total, ADHD, and ADHD+ ODD (244,58 ± 16,81 μm, 247,68±17,97 μm, and 241,26±15,38 μm respectively) have not found as statistically significant compared to the RNFL thickness detected in the control group (p> 0,05). This situation has not changed in the right eye measurements of the RNFL (Table 3). However, the lower values which are closeness to statistical significance in the left and right eye RNFL thicknesses of ADHD+ODD group compared to the control group (p-values= 0, 080 and 0.053 respectively), is remarkable.

The mean optical nerve thickness in the right eye inferior quadrant (134, 74±17,2 μm) of the control group found to be significantly higher than the patient group (126, 96±12, 4μm) (p= 0,040). Furthermore, left eye superior quadrant thickness (129,09±14, 5μm) and the average left optic nerve

Table 2. Comparison of ADHD and ADHD/ODD groups according to the scale scores.

	ADHD Sub-scales		ADHD (n=16)	ADHD+ODD (n=15)	P-value
	Oppositionality		9.4	24.8	0.000*
	Cognitive problems		23.4	27.4	0.05*
	Hyperactivity		16.3	21.5	0.000*
Conner's (Parent)	Anxiety		6.6	5.06	0.293
	Global Index		18.3	22.1	0.039*
	Perfectionism		5.1	5.6	0.921
	Social problems		5.6	6.1	0.905
	Psychosomatic		3.1	3.2	0.904
	Anxiety/impulsivity		14.4	17.5	0.007
	Emotional variability		3.8	4.6	0.322
	DSM-IV index	Inattention	18.8	21.2	0.107
		Hyperactivity/Impulsivity	18.0	22.4	0.003*
		Total	36.8	43.6	0.013*
Conner's (Teacher)	Oppositionality		2.8	14.1	0.000*
	Cognitive problems		13.5	14.2	0.217
	Hyperactivity		13.0	15.6	0.000*
	Anxiety		2.3	1.6	0.216
	Global Index		15.6	22.6	0.000*
	Perfectionism		1.5	1.2	0.724
	Social problems		3.8	9.3	0.000*
	ADHD Hyperactivity		9.3	12.7	0.000*
	Anxiety/impulsivity		11.2	12.8	0.002*
	Emotional variability		4.3	9.8	0.000*
	DSM-IV index	Inattention	19.7	21.6	0.214
		Hyperactivity/Impulsivity	16.9	22.2	0.000*
		Total	36.6	43.9	0.000*

***= p<0.05 statistically significant.**
****= All mean value comparisons for scale scores performed by Mann-Whitney U test.
ADHD: Attention Deficit Hyperactivity Disorder
ODD: Oppositional Defiant Disorder

thickness (104, 17±8, 7μm) of the control group were significantly higher than the patient group (121,51±12,6 μm, 99,52±6,9 μm) (p- values; 0.033, 0.015 respectively) (Tablo 3).

Total RNFL, GCL and optic nerve thickness measurements of both the left and the right eye; no statistically significant differences found between the ADHD and the ADHD+ ODD groups (p> 0,05).

In our study, only a weak negative correlation has detected between the left retina thickness and the Conners' Parent Cognitive Problems subscale; and between the average left optic nerve thickness and the Conners' Hyperactivity-Impulsivity subscale in the patient group. Besides, there was no statistically significant correlation found between the ophthalmic measurements and the symptom signs in the patient group.

DISCUSSION

ADHD is the most common psychiatric disorder in children. Being encountered three times more in male gender, although onset of ADHD is at the early ages, usually it is diagnosed in primary school period when the symptoms get more severe (19, 20). In accordance with these data, total ADHD+ODD group of patients in our study have been comprised of boys, additionally 81,2% (n=13) of the ADHD group were also boys.

Up to the present in the published data, lessening in the RNFL and macular thicknesses have been reported in neurological diseases as Alzheimer, Parkinson and MS (21-23). Recently, scope of the studies has been broadened to include psychiatric disorders; hence lessening of RNFL and macular thicknesses have been suggested in cases as schizophrenia, bipolar disorder, and autism spectrum disorder (24-26). Herguner et al have compared the RNFL thickness measurement results of 45 ADHD diagnosed children with a healthy group of 45 children; and they have found the RNFL thickness in the nasal quadrant of the ADHD diagnosed children to be significantly lower than the control group. Moreover, they have reported a negative correlation between the severeness of the symptoms and the RNFL thickness (27). In our study,

Table 3. Comparison of the ocular measurements between groups.

Ocular Measurements	Control (31)	Patients (Total)	Patients Group (31)		P-value[a]	P-value[b]
			ADHD (n=16)	ADHD+ODD (n=15)		
Left Retina Thickness	250,90±17,8	244,58±16,8	247,68±17,9	241,26±15,3	0.157	0.561
Right Retina Thickness	252,29±18,7	244,67±16,0	248,18±14,9	240,93±16,7	0.091	0.481
Right Ganglion Superior	100,15±5,5	95,79±2,9	96,06±3,0	95,5±2,9	**0.000***	0.936
Right Ganglion Inferior	101,56±5,3	96,89±2,9	96,73±2,9	97,06±2,9	**0.000***	0.922
Right Ganglion Total	100,84±5,2	96,31±2,7	96,39±2,8	96,21±2,6	**0.000***	0.992
Left Ganglion Superior	100,89±5,3	97,09±3,5	97,15±3,8	97,03±3,2	**0.002***	0.997
Left Ganglion Inferior	100,86±5,4	97,61±3,2	97,65±3,1	97,55±3,4	**0.006***	0.998
Left Ganglion Total	100,87±5,2	97,28±3,2	97,33±3,3	97,22±3,1	**0.002***	0.997
Right Optic Superior	118,00±12,6	122,41±14,3	118,68±10,3	126,40±17,1	0.242	0.212
Right Optic Inferior	134,74±17,2	126,96±12,4	125,68±13,5	128,33±11,3	**0.040***	0.692
Right Optic Temporal	80,38±9,4	76,8±10,1	77,18±12,8	76,46±6,5	0.160	0.845
Right Optic Nerve Nasal	80,22±9,9	81,29±12,4	82,87±14,8	79,60±9,6	0.712	0.475
Right Optic Nerve (Avg)	103,16±9,1	101,69±8,0	101,09±7,3	102,33±8,9	0.587	0.905
Left Optic Superior	129,09±14,5	121,51±12,6	120,62±9,4	122,46±15,7	**0.033***	0.698
Left Optic Nerv Inferior	128,32±14,3	121,64±12,6	123,31±11,9	119,86±13,5	0.057	0.458
Left Optic Temporal	80,87±10,5	78,03±14,6	77,00±16,4	79,13±12,7	0.077	0.373
Left Optic Nerve Nasal	77,96±7,9	76,67±9,8	73,93±8,4	79,60±10,6	0.572	0.111
Left Optic Nerve (Avg)	104,17±8,7	99,52±6,9	98,56±7,3	100,55±6,5	**0.015***	0.362

a=P-value calculated between control and total patients. (Independent Samples T-Test or Mann-Whitney U test).
b=P-value calculated between ADHD and ADHD/ODD groups (Independent Samples T-Test or Mann-Whitney U test).
*=P<0.05 statistically significant.
ADHD: Attention Deficit Hyperactivity Disorder
ODD: Oppositio nal Defiant Disorder

although a thinning in the left and right eye average RNFL thickness detected in the patient group, it was not statistically significant. Nevertheless, the fact that the difference detected in the left and right eye RNFL thickness measurements of the ADHD+ODD patients from the measurements of the control group has been found to be very close to statistical significance ($p=0.080$, $p=0.053$ respectively), is noteworthy. We could not get a statistically significant result because the study sample was small. Therefore, as stated in the study by Ascaso FJ. et al. with schizophrenia patients; they could not find a statistically significant difference between recent illness episode(RIE) patients and healthy controls. They stated a potential explanation for the negative ?ndings in RIE patients could be related to in?ammation resulting to increase retinal thickness in schizophrenia patients. This situation could be mentioned for our findings also. (24, 28). Furthermore, although no statistically significant effect of ODD comorbidity has been established through our study, we consider that, the RNFL thickness measurements we have established as close to statistical significance in the group with ODD comorbidity, confirmation of our findings in the future with extensive sampling groups is essential.

Psychiatric disorders such as major depressive disorder, ADHD, and autism spectrum disorder, studies have associated brain dysfunction with retinal abnormalities and have stated that it can be confirmed through ganglion cell layers(13). GCL, comprising of ganglion cells and being part of the retina have been reported now, to be thinner in psychiatric patients compared to healthy control groups by the researchers(29, 30). Similarly, Celik M. et al in their study conducted with 41 schizophrenic patients have reported GCL thickness volumes to be significantly lower than that of the control group; moreover, the GCL thickness volume measurements found to be even lower in the treatment resistant group (31). In our study, consistent the Celik et al.'s study, left and right eye superior and inferior quadrants and total GCL thickness measurements of the control group have been found to be significantly higher not only from the total patient group, but also from ADHD and ADHD+ODD groups separately in this study. However, based on total GCL thickness measurements, no statistically significant difference found between pure ADHD and ADHD+ODD groups. According to these findings, we could suggest that, comorbid ODD diagnosis is not an additional thinning to retinal fiber layer thickness compared to ADHD diagnosis. So, probably, comorbid ODD symptoms may influenced from environmental factors, as well as of biological and genetic factors. but since the sample size is small, this finding could not be generalized, only could add a new perspective to treatment options, those target social conditions and family structure.

Through embryonic development process, prosencephalon which will later form the optic nerve and the retina is differentiated in the optic saccule(12). Grönlund MA. et al have reported that abnormal ophthalmic symptoms were detected with a rate of 76%; and that, the symptoms included optic disc shrinkage and shrinkage in the optic rim areas in 42 ADHD diagnosed children. Furthermore, researchers have pointed out the morphological changes in the optic nerve and in the retinal vasculature. They have suggested that this originates from the retinal ganglion neurons and their extensions which set out from the optic nerve, hence the shrinkage in the neuroretinal area manifest itself in the optic nerve as the lessening of axons quantitatively or in volume (32). In contrast with these data, Mezer E. and Wygnanski - Jaffe T. have observed no morphological changes on the optic nerve and the retinal vasculature after a detailed ophthalmic examination of 32 ADHD, and 19 AD diagnosed (n=51) children (9). In accordance with the findings of Grönlund et al; patient group's average optic nerve thickness of the right eye inferior quadrant, as well as the optic nerve thickness of the left eye superior quadrant and the left eye optic nerve thickness found statistically lower than control group in our study. However no statistically significant difference found between the ADHD and ADHD+ODD group measurements when they compared for both eyes, for the thickness of optic nerve in the superior, inferior, temporal and nasal quadrants; and for the right eye optic nerve average thickness.

In conclusion, we able to evaluate the outcomes as, Ganglion cell layer of retina is thinner in patients with ADHD with/without ODD compared to

healthy controls. But this difference is not clear in between patients with ADHD and ADHD comorbid ODD. Comorbid ODD diagnosis is not an additional thinning to retinal fiber layer thickness compared to ADHD diagnosis. There is no correlation between retinal thinning and symptom severity.

The major limitation in our study is small study sample, so we could not generalize our findings. We collected all participants from near local areas. This sample could not reflect the general population. Technical problems could influence our results. (For example OCT machine brands etc.) Further studies are needed for clarify this difference.

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