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A Study on Changes in Retinal and Choroidal Structure in Children with Attention Deficit and Hyperactivity Disorder

Dikkat Eksikliği ve Hiperaktivite Bozukluğu Bulunan Çocuklarda Retina ve Koroid Yapısındaki Değişimler Üzerine Bir Araştırma

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ÖZET

Amaç: Bu çalışmada, Dikkat Eksikliği ve Hiperaktivite Bozukluğu (DEHB) tanısı almış çocuklarda, retina sinir lifi tabakası (RSLT), ganglion hücre tabakası (GHT) ve makular koroid kalınlığının optik koherens tomografi (OKT) kullanılarak değerlendirilmesi amaçlanmıştır.
Gereçler ve Yöntem: 2019 yılında yürütülen çalışmada, K-SADS psikometrik testi ile DEHB tanısı almış 30 çocuk ile yaş ve cinsiyet açısından eşleştirilmiş 30 sağlıklı kontrol grubu karşılaştırılmıştır. Tüm katılımcılara kapsamlı bir göz muayenesi uygulanmış; en iyi düzeltilmiş görme keskinliği, biyomikroskopi ve fundus muayenesi yapılmıştır. RSLT, GHT ve makular koroid kalınlıkları OKT ile ölçülmüş, gruplar arası farklar istatistiksel olarak analiz edilmiştir.
Bulgular: DEHB grubundaki bireylerin yaş ortalaması 9,90 ± 2,15 yıl, kontrol grubunda ise 9,10 ± 2,80 yıl olarak bulunmuş; iki grup arasında yaş ve cinsiyet açısından anlamlı fark saptanmamıştır ($p > 0.05$). OKT ile yapılan ölçümlerde, RSLT, GHT ve koroid kalınlıkları yönünden gruplar arasında anlamlı bir fark bulunmamıştır ($p > 0.05$).
Sonuç: Bu çalışma, DEHB'li bireylerde retinal ve koroidal yapılarda anlamlı yapısal değişiklik olmadığını göstermektedir. Bulgular, bu anatomik yapıların DEHB ile ilişkili olmadığını düşündürmektedir. Gelecekte yapılacak daha geniş örneklemli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Dikkat eksikliği hiperaktivite bozukluğu, retina, ganglion hücre tabakası, koroid, optik koherens tomografi

ABSTRACT

Objective: The aim of this study was to evaluate retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and macular choroidal thickness in children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) using optical coherence tomography (OCT).
Materials and Methods: Conducted in 2019, this study included 30 children diagnosed with ADHD using the K-SADS psychometric tool, along with 30 age and sex-matched healthy controls. All participants underwent full ophthalmologic examinations, including best corrected visual acuity, biomicroscopy, and fundus evaluation. OCT was used to measure RNFL, GCL, and macular choroidal thickness. Data were analyzed statistically to determine differences between the groups.
Results: The mean age was 9.90 ± 2.15 years in the ADHD group and 9.10 ± 2.80 years in the control group, with no significant difference ($p > 0.05$). Similarly, there were no statistically significant differences in terms of RNFL, GCL, or choroidal thickness between the two groups ($p > 0.05$).
Conclusion: The results indicate that structural changes in the retinal and choroidal layers are not prominent in children with ADHD. These findings suggest a lack of direct anatomical correlation. Further studies with larger populations are recommended to validate these results.

Keywords: Attention deficit hyperactivity disorder, retinal nerve fiber layer, ganglion cell layer, choroid, optical coherence tomography

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INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurocognitive disorder of childhood, with a reported prevalence ranging from 2% to 18% among children aged 6 to 17 years in developed countries (1–3). In a multicenter study conducted in Türkiye, the incidence of ADHD was reported to be 12.4% (4). ADHD is associated with difficulties in social, academic, cognitive, and emotional functioning (5). The core symptoms include inattention, hyperactivity, and impulsivity (6). The combined type of ADHD, which includes all three symptom domains, is considered the most common subtype (7). Neuroimaging studies have reported neuroanatomical and functional differences in individuals with ADHD compared to the normal population. Although the timing, specific regions, and characteristics of these morphological changes are not yet fully understood, ADHD is now classified as a neurodevelopmental disorder (8). During embryonic development, the optic nerve and retina differentiate from the diencephalon and are considered part of the central nervous system (9). Therefore, the retinal layer plays an important role in studies related to neurodevelopmental

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disorders.

Studies examining visual functions and ocular characteristics in children diagnosed with ADHD have addressed topics such as visual activity, strabismus, refractive errors, optic disc and retinal nerve fiber structure, and cognitive visual problems (10). The influence of the retina on the cognitive functions of individuals with ADHD has been observed. Histopathological studies have revealed a loss of retinal ganglion cells, while in vivo studies have reported thinning of the retinal nerve fiber layer (11).

Identifying and treating ocular problems in children diagnosed with ADHD may significantly improve their quality of life. Therefore, in this study, we aimed to compare retinal and choroidal changes in children diagnosed with ADHD to those in a control group.

MATERIALS AND METHODS

In 2019, two groups of participants were recruited from the Departments of Ophthalmology and Child and Adolescent Mental Health and Diseases of Sivas Cumhuriyet University Faculty of Medicine Hospital in Türkiye. The ADHD group consisted of patients diagnosed based on symptom history obtained from families presenting to the child and adolescent psychiatry outpatient clinic, observation of the child's current condition, and information gathered from schools and teachers, along with a supporting psychometric test. The psychometric assessment used was the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K-SADS). This test is a semi-structured interview designed to assess both current and past psychopathologies according to DSM-5 diagnostic criteria. Originally developed by Kaufman et al. in 1997 based on DSM-III and DSM-IV criteria, the interview schedule was updated in 2016 to align with DSM-5 diagnoses following the system's revision in 2013. The Turkish adaptation of the revised version, which includes both dimensional and categorical diagnostic evaluations, was validated and tested for reliability by Ünal et al. in 2018 (12).

The control group consisted of age- and sex-matched children who presented to the ophthalmology outpatient clinic for eye examinations, had no ocular disease history other than refractive errors, and did not have any psychiatric disorders. For each eye, patients with refractive errors greater than ± 3.0 diopters, axial eyeball length greater than 26 mm, cup-to-disc ratio greater than 0.3, cup-to-disc asymmetry between the two eyes greater than 0.2, history of eye surgery, glaucoma, uveitis, any eye with amblyopia, or children who had undergone treatment for retinopathy of prematurity were excluded from the study.

Ethical approval for the study was obtained. Additionally, written informed consent in accordance with the World Medical Association's Declaration of Helsinki was obtained from at least one parent or guardian of all children included in the study.

In the study, participants underwent detailed eye examinations, and optical coherence tomography (OCT) (OCT RS-3000 Advance, NIDEK CO. LTD., JAPAN) imaging was performed. The retinal nerve fiber layer (RNFL) thickness, ganglion cell layer (GCL) thickness, and macular choroidal thickness (MCT) were measured using OCT. The average RNFL thickness and the RNFL thickness in the four quadrants (nasal, temporal, superior, inferior) were recorded separately. RNFL thickness was measured in a 6×6 mm^2 area centered on the optic disc, while GCL thickness was measured in a 12×8 mm^2 area centered on the fovea. MCT was measured at five different points, in the region between the outer hyperreflective boundary of the retinal pigment epithelium and the inner scleral surface, subfoveal and 1 and 2 mm nasal and temporal to the fovea.

The data obtained from our study were entered into the SPSS 22.0 program. When the assumptions for parametric tests were met (Kolmogorov-Smirnov), the independent two-group comparisons were made using the t-test for the difference between two means. For the analysis of categorical data, the chi-square test was used, and the significance level was set at 0.05.

RESULTS

In the patient group, 9 (30%) were female and 21 (70%) were male, while in the control group, 10 (33.3%) were female and 20 (66.7%) were male. There was no significant difference between the groups in terms of gender ($p > 0.05$).

The mean age was 9.90 ± 2.15 years in the ADHD group and 9.10 ± 2.80 years in the control group. When comparing the individuals in both groups in terms of age, there was no statistically significant difference between the groups ($p > 0.05$).

The OCT measurements of 30 eyes from 30 children with ADHD were compared with 30 eyes from the control group. When comparing the individuals in both groups based on the RNFL thickness in the four quadrants, no statistically significant

Table 1. RNFL Thickness Values of Individuals

RNFL Thickness (Mean ± SD) (µm)	ADHD Group (n=30)	Control Group (n=30)	p value
Upper Quadrant	130.4±16.1	127.7±15.6	0.519
Nasal Quadrant	76.6±11.4	76.5±11.4	0.265
Lower Quadrant	137.8±17.1	137.9±16.3	0.221
Temporal Quadrant	70.5±9.8	71.7±10.9	0.587

Mean ± SD: Mean ± Standard deviation, µm = micrometer RNFL: Retinal Nerve Fiber Layer ADHD: Attention Deficit Hyperactivity Disorder

Table 2. GCL Thickness Values of Individuals

GCL Thickness (Mean±SD) (µm)	ADHD Group (n=30)	Control Group (n=30)	p value
Upper Quadrant	99.8±9.8	127.9±16.7	0.363
Lower Quadrant	100.5±10.1	97.9±9.8	0.324
Mean	100.2±9.6	97.7±8.2	0.302

Mean ± SD: Mean ± Standard deviation, µm = micrometer GCL: Ganglion Cell Layer ADHD: Attention Deficit Hyperactivity Disorder

Table 3. Choroid Thickness Values of Individuals

MCT (Mean±SD) (µm)	ADHD Group (n=30)	Control Group (n=30)	p value
Subfoveal choroidal thickness (µm)	390.6±66.8	379.6±61.3	0.510
Nasal 1 mm choroidal thickness (µm)	327.5±65.6	322.2±60.8	0.748
Nasal 2 mm choroidal thickness (µm)	293.3±66.8	290.5±59.0	0.861
Temporal 1 mm choroidal thickness (µm)	340.9±54.5	330.0±57.9	0.456
Temporal 2 mm choroidal thickness (µm)	321.0±51.1	311.0±58.2	0.483

MCT: Macular Choroidal Thickness Mean ± SD: Mean ± Standard deviation, µm = micrometer ADHD: Attention Deficit Hyperactivity Disorder

difference was observed ($p > 0.05$) (Table 1).

When comparing the GCL thickness in the upper, lower quadrants, and the average between the two groups, no statistically significant difference was observed ($p > 0.05$) (Table 2). When comparing the choroidal thickness in the subfoveal, nasal, and temporal regions between the two groups, no statistically significant difference was observed ($p > 0.05$) (Table 3).

DISCUSSION

ADHD is associated with various dysfunctions and abnormalities of the central nervous system. Numerous brain imaging studies have highlighted a cortical developmental delay in children with ADHD (13). In a long-term follow-up study, a maturation delay, especially in the prefrontal cortex and middle/upper temporal cortex, was observed in children with ADHD compared to the healthy group (13).

Both the retina and the brain areas responsible for cognitive functions originate embryonically from the prosencephalon. Considering this relationship, clinical studies have been planned, and results supporting the link between retinal-brain dysfunction and increased glaucoma prevalence in Alzheimer's patients have been obtained (14). Other supporting evidence comes from histopathological postmortem studies showing retinal ganglion cell loss in Alzheimer's patients (15) and in vivo studies (11,16). A reduced RNFL thickness has been reported in Alzheimer's patients (17).

In light of this information, we hypothesized that retinal area scanning, including retinal nerve fiber layer (RNFL) thickness, ganglion cell layer (GCL) thickness, and choroidal thickness, could be beneficial in ADHD patients. In our study, no significant difference was observed between the groups in terms of RNFL and GCL thickness. In a study by Bodur et al., involving 62 children, no significant difference in RNFL thickness was found between the ADHD and control groups, similar to our findings. However, in contrast, they found a thinner GCL thickness in the ADHD group compared to the control group (18). Hergüner et al. compared 45 ADHD patients with 45 controls in terms of RNFL thickness and found that the nasal quadrant was significantly thinner in the ADHD group compared to the control group. They also found a negative correlation between symptom severity and RNFL thickness (19). In the study by Işık et al., groups were formed as those receiving methylphenidate treatment, not receiving treatment, and healthy controls. When comparing the groups in terms of RNFL, GCL, and central macular thickness measurements, no statistically significant difference was found (20). Except for the study by Hergüner et al., no significant difference in RNFL thickness has been observed in clinical studies of children with ADHD, including our study. Işık et al. suggested that this might be due to ADHD being a neurodevelopmental rather than a neurodegenerative disorder (20).

Until now, a limited number of studies have been conducted on visual functions and ocular characteristics in patients with ADHD. In a study by Mezer et al., the frequency of ocular and visual function disorders was found to be higher (10). Additionally, it has been reported that the incidence of eye motility disorders and convergence insufficiency is also high in ADHD patients (21-23). Grönlund et al. detected abnormal ophthalmic symptoms in 76% of 42 children diagnosed with ADHD, including optic disc shrinkage and narrowing of the optic rim. Furthermore, the researchers pointed out morphological changes in the optic disc and retinal vasculature. They suggested that this may stem from the retinal ganglion neurons and extensions from the optic nerve, with the shrinkage in the neuroretinal area manifesting as a reduction in axons quantitatively or volumetrically in the optic nerve (24). In contrast to these findings, Mezer and Wygnanski-Jaffe, after detailed ophthalmic examinations of 32 children with ADHD and 9 children with other disorders, did

not observe any morphological changes in the optic nerve or retinal vasculature (10).

In this study, we compared the subfoveal and nasal and temporal choroidal thicknesses at 1 and 2 mm from the fovea between ADHD patients and the healthy control group. Similar to other studies, we found that the choroidal thickness was highest in the subfoveal area, decreasing as it moved away from the fovea, with thickness being greater in the temporal region.

In our study, children aged 5-16 years were included, and no significant difference was found between the patient and control groups in terms of age. Although no age stratification was performed, this suggests that the randomization of the cases included in the study was done appropriately.

Some studies have shown significant gender differences in choroidal thickness. Many studies have indicated that the choroid is thicker in men than in women. In a study by Barteselli et al., the choroidal thickness in men was found to be 7.4% greater than in women (25). This gender difference should be taken into account when performing EDI-OCT measurements. In this study, the groups were selected in such a way that there was no statistical difference in terms of gender. When comparing gender characteristics in the ADHD group, the proportion of males was found to be 70.0%, and females 30.0%. ADHD, which is more commonly seen in males, has been shown to have a male/female ratio ranging from 1/1 to 3/1 in population-based studies worldwide, while in clinical studies, this ratio can rise as high as 9/1 (26, 27). A large meta-analysis conducted in 2007 found the male/female ratio to be 4/1 (28). The findings regarding the gender-ADHD relationship in our study are consistent with those of other studies.

The limiting factors in our study include the relatively small sample size, the inclusion of children in the control group without excluding ADHD diagnosis, and the lack of analysis based on medication use in the ADHD group.

CONCLUSION

OCT, a modern measurement technique that allows for the comparison of pathologies with objective measurements, was difficult to use due to cooperation issues in the pediatric age group, but despite all the challenges with this age group, it was successfully utilized, allowing us to obtain valuable data. In light of these findings, despite various limitations, we believe our study will contribute to the literature.

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