



# Optic Nerve Head Parameters, Retinal Nerve Fiber Layer and Executive Functions in Children with Attention Deficit Hyperactivity Disorder

Dikkat Eksikliği Hiperaktivite Bozukluğu Olan Çocuklarda Optik Sinir Başı Parametreleri, Retina Sinir Lifi Tabakası ve Yönetici İşlevler

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## ABSTRACT

**Aim:** This study aimed to evaluate the relationship between executive functions and optic nerve head parameters (the disc area, the neuroretinal rim volume and cup-to-disc ratio) and peripapillary retinal nerve fiber layer (pRNFL) in medication-free school-age children diagnosed with (ADHD).

**Materials and Methods:** Thirty children aged 8-12 years, who were diagnosed with ADHD, and thirty healthy children without psychiatric disorders were included in the study. Parents of all participants filled out the Sociodemographic Data Form, the Behavior Rating Inventory of Executive Function (BRIEF) Parent form, and the Conners Parent Rating scale. All children underwent a comprehensive eye examination. Optic nerve head parameters and pRNFL were measured using optical coherence tomography.

**Results:** The BRIEF subscale, which evaluates executive functions, showed a significant difference between children diagnosed with ADHD and the control group ( $p<0.05$ ). In the left eye, the nasal pRNFL region thickness, the disc area and neuroretinal rim volume width were found to differ between the groups ( $p<0.05$ ). Both optic nerve rim volume and disc area were negatively correlated with BRIEF subscales, including initiation, working memory, organization, monitoring, metacognitive index, and global executive index scores. However, no relationship was found between pRNFL thickness (nasal) in the left eye and the BRIEF subscales.

**Conclusion:** This novel study has shown a potential relationship between optic nerve head parameters and executive functions in children diagnosed with ADHD. Further studies using performance-based tests and neuroimaging devices (functional magnetic resonance imaging) are needed to examine the relationship of optic nerve head parameters with executive functions in ADHD.

**Keywords:** Optic nerve head parameters, retinal nerve fiber layer, executive functions, ADHD

## ÖZ

**Amaç:** Çalışmamızda, dikkat eksikliği hiperaktivite bozukluğu (DEHB) tanısı almış, ilaç kullanmayan okul çağındaki çocuklarda yönetici işlevler ile optik sinir başı parametreleri (optik disk alanı, nöroretinal rim hacmi ve çukurluk disk oranı) ve peripapiller retina sinir lifi tabakası kalınlığı (pRNFL) arasındaki ilişkinin değerlendirmesi amaçlanmıştır.

**Gereç ve Yöntem:** Çalışmamıza DEHB tanısı alan, 8-12 yaş arası otuz çocuk ile herhangi bir hastalığı (göz, psikiyatri, metabolik ve diğer) olmayan ve ilaç tedavisi almayan otuz sağlıklı çocuk dahil edilmiştir. Tüm katılımcıların ebeveynleri, Sosyodemografik Veri Formu, Yönetici İşlevlere Yönelik

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Davranış Değerlendirme Envanteri (YİDDE) Ebeveyn formu ve Conners Ebeveyn Değerlendirme ölçeğini doldurmuştur. Tüm çocuklara kapsamlı bir göz muayenesi yapıldı ve optik koherens tomografi kullanılarak optik sinir başı parametreleri ve pRNFL ölçüldü.

**Bulgular:** Yönetici işlevleri değerlendiren YİDDE alt ölçeği, DEHB tanısı alan çocuklarda anlamlı fark bulundu ( $p<0,05$ ). Her iki grup arasında sol gözde, nazal pRNFL bölge kalınlığı, optik disk alanı ve nöroretinal rim hacmi istatistiksel farklılık gösterdi ( $p<0,05$ ). Ayrıca, optik sinir nöroretinal rim hacmi ve optik disk alanı ile başlatma, çalışma belleği, organizasyon, izleme, metakognitif indeks ve genel yönetici indeks gibi YİDDE alt ölçekleri arasında negatif yönlü bir ilişki saptandı.

**Sonuç:** Bu çalışma, DEHB tanısı almış çocuklarda optik sinir başı parametreleri ile yönetici işlevler arasında potansiyel bir ilişki olabileceğini göstermiştir. Optik sinir başı parametrelerinin DEHB'deki yönetici işlevlerle ilişkisini incelemek için performansa dayalı testler ve nörogörüntüleme cihazları (fonksiyonel manyetik rezonans görüntüleme) ile yapılan daha fazla çalışmaya ihtiyaç vardır.

**Anahtar Kelimeler:** Optik sinir başı parametreleri, retina sinir lif tabakası, yönetici işlevler, DEHB

## INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by the symptoms of inattention, hyperactivity, and impulsivity that are not developmentally appropriate and negatively affect psychosocial functioning<sup>1</sup>. As the most common psychiatric disorder of childhood, the prevalence of ADHD worldwide varies between 1.7% and 17.8%, with recent epidemiological studies reporting a median prevalence of 4% in children and adolescents<sup>2</sup>. In a study conducted in Türkiye by Ercan et al.<sup>1</sup>, the prevalence of ADHD was found to be 12.7%. Executive functions (EFs) encompass a range of cognitive skills necessary for the purposeful planning and execution of thoughts and behaviors, including directing attention, inhibiting inappropriate stimuli (inhibition), maintaining active information, and ensuring the transition among information<sup>3</sup>. Working memory, inhibition, and cognitive flexibility are core components of EFs<sup>3</sup>. In the existing literature, numerous studies have utilized different neuropsychological tests to assess EFs in children with ADHD<sup>4</sup>. Meta-analyses have consistently found weaker EF skills in children diagnosed with ADHD, including deficits in inhibition, sustained attention, working memory, and cognitive flexibility<sup>4</sup>.

The retina originates from the cerebral cortex and embryological prosencephalon, containing unmyelinated axons and glial cells<sup>5</sup>. Due to these factors, it is believed that changes in the structure and function of the brain may be reflected in the retina<sup>5</sup>. Optical coherence tomography (OCT) is a non-invasive and non-contact imaging technique that provides cross-sectional images of retinal tissue<sup>6</sup>. OCT enables the measurement of peripapillary retinal nerve fiber layer (pRNFL), ganglion cell layer (GCL), and macular thickness, which can be used to monitor and assess treatment response in ophthalmic diseases such as glaucoma and macular disorders<sup>7</sup>. In recent years, studies have examined pRNFL, GCL, and macular thickness in certain psychiatric disorders such as bipolar disorder, ADHD<sup>8-11</sup>, and autism spectrum disorder (ASD)<sup>12</sup>, and have revealed differences. Additionally, OCT has been reported to detect chronic axonal degeneration and structural abnormalities in the central nervous system<sup>13</sup>.

In neuroimaging studies on the etiology of ADHD, it has been observed that cases diagnosed with ADHD have atypical brain structure. In these cases, a decrease in total brain volume has been reported in the prefrontal cortex (PFC), basal ganglia, cerebellum, and parietotemporal areas<sup>14</sup>. However, in a meta-analysis study evaluating studies examining the retinal features (pRNFL and GCL) of cases diagnosed with ADHD, it was found that there was a decrease in global peripapillary RNFL thickness and thinning in the GCL layer<sup>10</sup>. Additionally, literature has shown a negative correlation between frontal and parietal cortical thickness and EFs in childhood and adolescence (healthy individuals)<sup>15,16</sup>. Although the relationship between cortical thickness and EFs is not clear, it has been suggested that this difference between childhood and adulthood may be related to central nervous system maturation<sup>17</sup>. When the literature is examined, it is seen that many studies, in which EFs such as response inhibition, working memory and visuospatial perception were evaluated with functional brain imaging techniques, have reported increased activation in the dorsolateral PFC and parietal cortex<sup>18</sup>. In a study conducted with 1485 healthy volunteers, evaluating the relationship between RNFL thickness and cognitive functions, it was shown that RNFL thickness was significantly higher in people with better neuropsychological test scores<sup>19</sup>.

This study aimed to evaluate the relationship between EFs and optic nerve head (ONH) parameters (the disc area, the neuroretinal rim volume and cup-to-disc ratio) and pRNFL in medication-free school-age children diagnosed with ADHD.

## MATERIALS AND METHOD

### Sample

Our study included 30 children aged 8-12 years, diagnosed with ADHD according to DSM-V-TR, who sought treatment at the child and adolescent psychiatry outpatient clinic. Additionally, 30 healthy children without any psychiatric disorders were recruited. Additionally, individuals with any acute or chronic diseases related to neurology, genetics, endocrinology, infection, or the cardiovascular system were excluded. Additionally, those with known eye diseases

(especially glaucoma and ocular hypertension) and those using medication, except for  $\pm 2$  spherical refractive error, were also excluded. Participants whose parents did not consent to participate were also not included in the study. The study received approval from Erzurum Regional Training and Research Hospital Ethics Committee (decision no: 2022/13-140, date: 05.09.2022). Prior to the study, written and verbal informed consent was obtained from the parents of all participants.

## Procedure

Parents of all participants were asked to fill out a Sociodemographic Data form, the Behavior Rating Inventory of Executive Function Parent (BRIEF) form, and the Conners' Parent Rating Scale (CPRS) Short Form. A detailed eye examination was conducted on all 60 children participating in the study to exclude ophthalmological pathologies. Each participant underwent measurements of refractive errors using an autorefractometer, determination of best-corrected visual acuity with a Snellen chart, intraocular pressure measurement using Goldmann applanation tonometry, and a detailed ophthalmic examination including slit-lamp biomicroscopy and dilated fundus examination. Subsequently, non-invasive OCT measurements of both eyes were performed using the RTvue device (Optovue, CA, USA). Based on the study by Pitkänen et al.<sup>20</sup>, only measurements of pRNFL thickness (superior, inferior, nasal, and temporal region thickness) and ONH parameters (the disc area, the neuroretinal rim volume, and cup-to-disc ratio) of the left eye were included in the evaluation for each participant.

## Data Collection Tools

**Sociodemographic Data Form:** This form, prepared by the researchers, was designed and implemented to collect information about participants and family members (age, gender, delivery time, delivery type, developmental milestones (walking, talking, toilet training), family structure, and settlement).

**Hollingshead-Redlich Scale:** The Hollingshead-Redlich scale evaluates socioeconomic status (SES) by considering parental education and occupation. It categorizes SES into five levels, with the highest-achieving parent determining the score. Levels 1 and 2 denote high SES, Level 3 corresponds to middle SES, and Levels 4 and 5 indicate low SES<sup>21</sup>.

**Conners' Parent Rating Scale Short Form:** The Conners' rating scale is the most widely used behavior rating scale to assess the characteristics of ADHD in children and adolescents with sub-scales for inattention, hyperactivity, and oppositional behavior. The scale has been adapted into Turkish by Kaner et al.<sup>22</sup> Parents were asked to rate their children's behaviors on a four-point Likert scale for each item. The scale is scored as

never (0), rarely (1), often (2), and always (3)<sup>22</sup>. In our study, the ADHD index calculated from the scale utilized the Inattention and Hyperactivity subscales. The obtained high scores indicate the severity of ADHD symptoms.

**Behavior Rating Inventory of Executive Function Parent Form: BRIEF** was developed to assess EFs, problem-solving skills, and adaptive behaviors in children. This scale is filled out by an individual familiar with the child (parent, teacher) based on the child's behavior and attitudes over the last 6 months. The scale consists of a total of 86 items, and 8 subscale and 3 index scores related to a person's EFs can be calculated. The obtained high scores indicate weak executive skills. The Turkish standardization of the scale was conducted by Batan et al.<sup>23</sup>. The description of BRIEF Subscales is as follows<sup>23</sup>:

**Inhibition:** The capacity to regulate impulses and halt one's behavior at appropriate moments.

**Shifting:** The ability to transition flexibly between different situations, tasks, perspectives, or aspects of a problem.

**Emotional Control:** The skill of managing and regulating emotional responses.

**Initiate:** The ability to independently begin tasks or activities and generate ideas.

**Working Memory:** The capacity to hold and manipulate information in mind to complete tasks or respond appropriately.

**Planning/Organizing:** The ability to anticipate future events, set goals, create structured steps in advance, execute tasks systematically, and effectively communicate key ideas.

**Organization of Materials:** The ability to manage task-related demands while considering both present and future situational requirements.

**Monitoring:** The capacity to oversee work, assess performance, and track both one's own and others' efforts.

**Behavioral Regulation Index (BRI):** A composite score derived from the inhibition, shifting, and emotional control subscales.

**Metacognition Index (MCI):** A total score encompassing the initiate, working memory, planning/organizing, organization of materials, and monitoring subscales.

**Global Executive Composite Index:** Calculated as the sum of the BRI and MCI scores.

**OCT Measurement and Device Specifications:** Measurements were made using the RTvue device (Optovue, CA, USA) employing a non-invasive technique that provides tomographic sections of tissues at the micron level by measuring the reflection, delay time, and intensity of infrared light at approximately 840 nm wavelength sent to

tissues and reflected from different tissues. A detailed eye examination was conducted for each participant to exclude ophthalmological pathologies. During measurement, low-quality scans were rejected. All image qualities were controlled using the signal strength index (SSI). Only scans with SSI >50 were included in the study. For RNFL thickness measurements, a three-dimensional (3D) disc and a 4 mm diameter ONH map were used. pRNFL thickness measurements were obtained along 13 circular B-scans manually positioned over the optic disc to create a peripapillary RNFL thickness map. The pRNFL thickness measurement was calculated as the difference in distance between the inner limiting membrane and the outer edge of the inner plexiform layer within a circle with a diameter of 3.45 mm. The ONH scan provides a 3D view and is created using 12 radial B-scans with a fixed length of 3.7 mm for ONH shape analysis. In each scan series, average pRNFL thickness, quadrant pRNFL thickness (superior, inferior, temporal, and nasal), and optic disk volume and cup-disk areas with the cup-to-disk ratio were analyzed. Data were recorded with information about race, age, and gender. The device's recorded normative database outputs show color-coded normal distribution percentages among individuals of the same age. The lower 1% of normal measurements is shown in red, the lower 5% in yellow, the upper 5% in white, and the remaining 90% in green. Results were analyzed based on this information<sup>6</sup>.

## Statistical Analysis

The statistical analysis was performed using SPSS 23.0 statistical software package. Descriptive statistics of the evaluation results were presented as numbers and percentages for categorical variables and as mean, standard deviation, minimum, and maximum for numerical variables. The Kolmogorov-Smirnov test was used to assess the normal distribution conditions of the data. When the normal distribution condition was met for comparing numerical variables among three or more independent groups, the ANOVA test was used; otherwise, the Kruskal-Wallis test was used; otherwise, the Kruskal-Wallis test was used; otherwise, the Kruskal-Wallis Variance analysis was used. The Bonferroni test from post-hoc test statistics was employed to determine the source of significant differences among more than two groups. Spearman's rank correlation coefficient was used to analyze the relationship between numerical variables in two groups. The chi-square test was employed to analyze the differences in the proportions of categorical variables between independent groups. A significance level of  $p < 0.05$  was accepted for statistical significance.

## RESULTS

A total of 60 children aged between 8 and 12 years participated in the study. The groups were comparable in terms of age, gender, years of education, and SES ( $p > 0.05$ ) (Table 1). Significant differences were observed in the BRIEF subscale,

**Table 1. Sociodemographic characteristics of the participants, RNFL thicknesses, and ONH parameters**

	Children with ADHD (mean $\pm$ SD)	Controls (mean $\pm$ SD)	p-value
Age (years)	9.63 $\pm$ 1.93	9.23 $\pm$ 1.35	0.68 <sup>*</sup>
Gender (boy/girl)	22/8	16/14	0.108
Education (year)	4.37 $\pm$ 1.75	4.85 $\pm$ 2.71	0.887 <sup>*</sup>
Hollingshead-Redich scale (mean $\pm$ SD)	3.47 $\pm$ 1.22	3.76 $\pm$ 1.1	0.197 <sup>*</sup>
<b>CPRS</b>			
Inattention	9.8 $\pm$ 2.7	1.4 $\pm$ 1.3	<0.001 <sup>*</sup>
Hyperactivity	10.3 $\pm$ 7.22	1.16 $\pm$ 1.2	<0.001 <sup>*</sup>
ADHD index	14.7 $\pm$ 3.13	3.06 $\pm$ 1.8	<0.001 <sup>*</sup>
<b>pRNFL</b>			
pRNFL superior ( $\mu$ m) L	121.32 $\pm$ 9.90	125.41 $\pm$ 17.29	0.285 <sup>*</sup>
pRNFL inferior ( $\mu$ m) L	122.93 $\pm$ 11.52	125.67 $\pm$ 13.41	0.424 <sup>**</sup>
pRNFL temporal ( $\mu$ m) L	75.25 $\pm$ 8.92	77.9 $\pm$ 11.03	0.427 <sup>**</sup>
pRNFL nasal ( $\mu$ m) L	71.82 $\pm$ 6.41	75.59 $\pm$ 7.07	<b>0.043<sup>*</sup></b>
<b>Optic nerve head parameters</b>			
Optic disc area (mm <sup>2</sup> ) L	2.04 $\pm$ 0.50	2.27 $\pm$ 0.36	<b>0.048<sup>*</sup></b>
Optic neuroretinal rim volume (mm <sup>3</sup> ) L	1.51 $\pm$ 0.31	1.84 $\pm$ 0.39	<b>0.001<sup>**</sup></b>
Optic cup-to-disc ratio L	0.24 $\pm$ 0.16	0.19 $\pm$ 0.11	0.245 <sup>**</sup>

ADHD: Attention deficit hyperactivity disorder, p: Probability of significance,  $p < 0.05$ ,  $\mu$ m: Micrometers (data in the table presented in units of), pRNFL: Peripapillary retinal nerve fiber layer, L: Left eye, SD: Standard deviation, CPRS: Conners' parent rating scale, \*Kruskal-Wallis, \*\*ANOVA, ONH: Optic nerve head

which assesses EFs, between children diagnosed with ADHD and the control group ( $p<0.05$ ) (Table 2). When examining pRNFL and ONH parameters between the groups, differences were observed in the pRNFL nasal region thickness in the left eye ( $p=0.043$ ), the disc area belonging to the ONH ( $p=0.048$ ), and the neuroretinal rim volume ( $p=0.01$ ) (Table 1). Both optic neuroretinal rim volume and disc area showed a negative correlation with the sub-scores of the BRIEF scale, including initiation, working memory, plan/organize, organization of materials, monitoring, metacognitive index, and global executive composite index scores (Table 3). However, there was no relationship found between the pRNFL thickness (nasal) in the left eye and BRIEF subscales. Additionally, the ADHD index score calculated from the CPRS scale exhibited a negative correlation with both optic neuroretinal rim volume and optic disc area (Table 3).

## DISCUSSION

In recent years, studies investigating RNFL and optic nerve parameters using OCT in psychiatric disorders have started to increase. In the study, children diagnosed with ADHD exhibited significant differences in pRNFL nasal region thickness, optic disc area, and neuroretinal rim volume compared to the control group. Additionally, optic disc area and neuroretinal rim volume were found to be associated with BRIEF subscales in the ADHD group.

In the study, it was observed that both the optic disc area and the neuroretinal rim volume were thinner in the ADHD-diagnosed group ( $p<0.05$ ). Furthermore, these parameters of the left eye's ONH were found to be associated with both EFs, including initiation, working memory, plan/organize, organization of materials, monitoring, metacognition index and global

executive composite scores, and also the ADHD index score. In other words, it was found that children diagnosed with ADHD who had a larger optic disc area and neuroretinal rim volume exhibited stronger EFs skills and less severe ADHD symptoms. Studies in the literature that examine the relationship between ocular findings and cognitive impairment have reported controversial results. In a cohort study, Pitkänen et al.<sup>20</sup> found that individuals with a larger optic disc area had a higher level of education, completed the Humphrey 24-2 perimetric test (HFA) in a less time, but performed worse on the grade point average (GPA) test. In the same study, greater neuroretinal volume was detected to be associated with higher GPA, shorter HFA completion time, and fewer errors in the paired associates learning test. Similarly, in the Beijing Eye Study, the average age of the population was  $56.2\pm 10.6$  years, and it was emphasized that optic disc head size was associated with education level and perimetric test duration time. The author noted that education level was significantly associated with increasing disc size and shorter perimetric test duration<sup>24</sup>. Another study found that a larger optic cup-to-disc ratio in females was independently associated with poorer cognitive abilities<sup>25</sup>. The data obtained in our study are consistent with the findings of Pitkänen et al.<sup>20</sup> and Jonas et al.<sup>24</sup>. This interpretation suggests that an increase in both optic disc size and neuroretinal rim volume may be associated with stronger EFs skills and fewer symptoms in children diagnosed with ADHD. Since existing studies in the literature have primarily been conducted on adult populations, there is a need for more OCT studies with larger sample sizes in children with ADHD, assessing EF skills using diverse methodologies.

ADHD has been linked to dysfunctions in somatomotor and visual networks, alongside impairments in higher-level

**Table 2. Comparison of behavior rating inventory of executive function, of children with ADHD and controls**

	Children with ADHD (mean $\pm$ SD)	Controls (mean $\pm$ SD)	p-value
<b>BRIEF</b>			
Inhibition	24.40 $\pm$ 14.15	16.43 $\pm$ 7.6	<b>0.009*</b>
Shifting	15.6 $\pm$ 4.17	13.6 $\pm$ 1.74	<b>0.005*</b>
Emotional control	21.52 $\pm$ 5.08	16.35 $\pm$ 4.23	<b>&lt;0.001*</b>
Initiate	15.83 $\pm$ 3.04	11.85 $\pm$ 3.30	<b>&lt;0.001*</b>
<b>Working memory</b>	24.35 $\pm$ 3.40	17.08 $\pm$ 4.68	<b>&lt;0.001*</b>
Plan/organize	33.09 $\pm$ 7.53	21.69 $\pm$ 6.57	<b>&lt;0.001*</b>
Organization of materials	16.39 $\pm$ 4.35	11.73 $\pm$ 3.36	<b>&lt;0.001*</b>
<b>Monitoring</b>	18.35 $\pm$ 3.71	12.23 $\pm$ 3.69	<b>&lt;0.001*</b>
Behavioral Regulation index	73.26 $\pm$ 14.76	52.12 $\pm$ 11.38	<b>&lt;0.001*</b>
<b>Metacognition index</b>	91.61 $\pm$ 15.30	62.85 $\pm$ 16.90	<b>&lt;0.001*</b>
Global executive composite	164.87 $\pm$ 27.19	114.96 $\pm$ 26.91	<b>&lt;0.001*</b>

p: Probability of significance,  $p<0.05$ , ADHD: Attention deficit hyperactivity disorder, BRIEF: Behavior Rating Inventory of Executive Function, SD: Standard deviation, \*Independent sample t test



**Table 3. Correlation between properties of ONH, pRNFL (nasal) and the BRIEF scale**

	L optic neuroretinal rim volume	L optic disc area	L optic pRNFL nasal (µm) L
<b>BRIEF</b>			
Inhibition	p=0.588 r=-0.075	p=0.010 r=-0.344*	p=0.041 r=-0.276
Shifting	p=0.072 r=-0.271	p=0.028 r=-0.328*	p=0.827 r=-0.034
Emotional control	p=0.242 r=-0.178	p=0.133 r=-0.228	p= 0.371 r=-0.137
Initiation	<b>p=0.003 r=-0.436**</b>	<b>p&lt;0.001 r=-0.543**</b>	p= 0.327 r=-0.149
<b>Working memory</b>	<b>p=0.005 r=-0.415**</b>	<b>p=0.005 r=-0.408**</b>	p=0.129 r=-0.230
Plan/organize	<b>p=0.01 r=-0.378*</b>	<b>p=0.013 r=-0.366*</b>	p=0.264 r=-0.170
Organization of materials	<b>p&lt;0.001 r=-0.478**</b>	<b>p&lt;0.001 r=-0.500**</b>	p=0.125 r=-0.232
<b>Monitoring</b>	<b>p=0.02 r=-0.442**</b>	<b>p=0.003 r=-0.443**</b>	p=0.094 r=-0.253
Behavioral Regulation index	p=0.24 r=-0.336	p=0.016 r=-0.358*	p=0.122 r=-0.234
<b>Metacognition index</b>	<b>p=0.003 r=-0.435**</b>	<b>p=0.002 r=-0.445**</b>	p=0.165 r=-0.211
Global executive composite	<b>p=0.005 r=-0.409**</b>	<b>p=0.004 r=-0.425**</b>	p=0.128 r=-0.230
<b>CPRS</b>			
Inattention	<b>p=0.003 r=-0.428**</b>	p=0.016 r=-0.350*	p=0.297 r=-0.157
Hyperactivity	<b>p=0.011 r=-0.370*</b>	p=0.102 r=-0.241	p=0.576 r=-0.085
ADHD index	<b>p=0.001 r=-0.459**</b>	<b>p=0.009 r=-0.376**</b>	p=0.220 r=-0.184

ADHD: Attention deficit hyperactivity disorder, CPRS: Conners' Parent Rating scale, pRNFL: Peripapillary retinal nerve fiber layer, L: Left eye, SD: Standard deviation, ONH: Optic nerve head, p: Probability of significance, p<0.05, BRIEF: Behavior Rating Inventory of Executive Function Parent

cognitive and behavioral functions. Neurotransmitters such as dopamine, glutamate, and GABA play a crucial role not only in retinal function but also in post-ocular structures like the thalamus and visual cortex<sup>26</sup>. Research has shown that ADHD is associated with decreased GABA levels and increased glutamate levels in the PFC and striatum, alongside disruptions in dopaminergic signaling<sup>27</sup>. Dopamine is known to support retinal function in multiple ways, whereas glutamate, when present in excess, acts as a neurotoxin that damages retinal GCL. Notably, studies have found a significant reduction in RNFL thickness in parkinson's disease, where dopamine levels are diminished<sup>28</sup>. Similarly, retinal layer thinning has been observed in adults with restless legs syndrome, a condition frequently comorbid with ADHD and sharing overlapping pathophysiological mechanisms with parkinson's disease<sup>26</sup>. Some studies indicate that pRNFL thickness does not show a significant difference in children diagnosed with ADHD compared to the control group<sup>8,29,30</sup>, while others have observed thinning in pRNFL nasal quadrant thickness in individuals with ADHD<sup>9,31</sup>. In a study on ASD, the author interpreted the differences in pRNFL thinning in children diagnosed with ASD as an indicator of atypical brain development<sup>12</sup>. In our study, consistent with the findings of Hergüner et al.<sup>9</sup> and Kaymak et al.<sup>31</sup>, a significant reduction in the nasal quadrant thickness of pRNFL was observed in children diagnosed with ADHD (p<0.05). However, no significant association was observed between this difference and the ADHD index score. When evaluating pRNFL and ONH findings together, this difference in ONH structure may be attributed to variations in axonal volume, deficiencies in dopaminergic function, or structural

abnormalities in glial cells among children with ADHD. However, to better elucidate the underlying mechanisms of these alterations, further studies with larger sample sizes incorporating neuroimaging techniques and biochemical markers related to dopamine function are warranted.

In recent years, studies conducted on adult samples have found a relationship between pRNFL thickness and cognitive function<sup>19,32</sup>. Additionally, one of these studies has emphasized that macular GCL thickness is more strongly linked to cognitive functions than pRNFL thickness<sup>32</sup>. This relationship observed in the healthy population has also been evaluated in neurodegenerative diseases such as parkinson's disease and multiple sclerosis<sup>33,34</sup>. Thinning in pRNFL inferior quadrant thickness has been specifically associated with cognitive impairment in parkinson's patients<sup>33</sup>. In multiple sclerosis patients, changes in both pRNFL and GCL inner plexiform layer may be associated with cognitive impairment, suggesting a connection to neurodegeneration<sup>34</sup>. Another study investigated the relationship between EF skills, also known as advanced cognitive skills, and pRNFL in adults diagnosed with ADHD, like our study, and found no relationship between pRNFL and EFs<sup>31</sup>. The varied results in studies investigating the relationship between pRNFL and cognitive function in the literature may arise from differences in the scales used in the studies, the variability in age groups and the differences in the etiology of neurodegenerative diseases and neurodevelopmental disorders. To investigate the relationship between pRNFL and cognitive function, studies with larger samples in a similar age group within neurodevelopmental disorders are needed.

## Study Limitations

The present study has some limitations. One is its small sample size. The other is that the scale used to assess EFs in our study relies on parental feedback. Further studies with large samples are needed using performance-based tests and neuroimaging devices such as functional magnetic resonance imaging.

## CONCLUSION

In conclusion, our study is important as the first investigation of EFs and OCT parameters in school-age children diagnosed with ADHD. In school-age children with ADHD in our study, ONH parameters, specifically were found to be smaller and associated with poorer EF skills. On the other hand, pRNFL was only found to be thinner in the nasal quadrant in children with ADHD, and no relationship was found with EF skills. In the etiopathogenesis of ADHD, which is a neurodevelopmental disorder, changes in optic nerve parameters such as optic disc area and neuroretinal rim volume rather than pRNFL may suggest the indicators of atypical brain development. Therefore, we hope that our study will provide clinicians with a different perspective and serve as a guide in this regard.

## Ethics

**Ethics Committee Approval:** The study received approval from Erzurum Regional Training and Research Hospital Ethics Committee (decision no: 2022/13-140, date: 05.09.2022).

**Informed Consent:** Prior to the study, written and verbal informed consent was obtained from the parents of all participants.

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## Footnotes

## Authorship Contributions

Concept: G.Y.T., B.S.Ö., G.Ö., B.U., B.Ş., Design: G.Y.T., B.S.Ö., G.Ö., B.Ş., Data Collection or Processing: G.Y.T., B.U., B.Ş., Analysis or Interpretation: G.Y.T., B.S.Ö., G.Ö., A.Ç., B.U., B.Ş. Literature Search: G.Y.T., B.S.Ö., G.Ö., AB.U., B.Ş., Writing: G.Y.T., B.S.Ö., B.Ş.

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