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Optical Coherence Tomography Findings in Obsessive Compulsive Disorder: A Preliminary Receiver Operating Characteristic Analysis On Ganglion Cell Layer Volume for Neurodegeneration

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Abstract

Background: Many theories have been proposed to explain the etiology of obsessive compulsive disorder (OCD), but neuroimaging studies suggest neurodegeneration as a possible cause. Neurodegenerative diseases may cause a reduction in the retinal nerve fiber layer (RNFL) and the ganglion cell complex (GCC), and these changes can be detected by optical coherence tomography (OCT). The aim of this study was to examine the potential relationship between OCT findings and the clinical features of patients with OCD versus the findings for a healthy control (HC) group.
Methods: Patients with OCD (n=42) and HC subjects (n=50) completed sociodemographic, Beck Anxiety Inventory, and Beck Depression Inventory forms and underwent OCT. Patients undertook clinical interviews for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (SCID-I) and Yale-Brown Obsessive Compulsive Scale scores, whereas the HC group interviews used the SCID non-patient version.
Results: The RNFL and GCC values were significantly lower in the OCD than in the HC group ($p<0.05$). The GCC mean value indicated a significant and independent effect in distinguishing the OCD from the HC group ($p<0.05$). A significant positive correlation was observed between the age of onset of OCD and the GCC mean value ($p<0.05$). A significant negative correlation was observed between the untreated duration and the GCC mean value ($p<0.05$).
Conclusions: Neurodegeneration may manifest itself particularly as changes in the GCC volume and RNFL, and treatment may be neuroprotective in OCD. These findings may have implications for the neurobiology of OCD, its treatment considerations, and the course of the disease.

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by recurrent intrusive thoughts and repetitive behaviors or mental acts that usually persist throughout life, with occasional exacerbations [1]. OCD is a potential cause of impairment of social and occupational functioning and has an average incidence of 2% in the general population. Many theories have been proposed to explain the etiology of OCD, but growing evidence, especially from neuroimaging studies, now suggests neurodegeneration as a cause.

Previous studies have documented an association between OCD and abnormalities in neuroanatomical structures in the cortical-striatal-thalamic-cortical circuit [2]. For example, a neuroimaging study showed that patients with OCD might suffer from orbitofrontal–limbic–basal ganglia dysfunction [3], while another study found that neuropsychological tests indicate frontal lobe dysfunction, suggesting that dysfunction with possible right cerebral involvement might be important for understanding the etiology of OCD [4]. Magnetic resonance spectroscopy (MRS) studies have indicated that patients with OCD show decreases in various brain metabolites, including creatine-phosphocreatine (a cellular energy marker), N-acetyl-aspartate (a neuronal viability marker), myo-inositol, glutamine, and choline (a cell membrane turnover marker), and this can indicate a loss of axons or neurons [5]. A decrease in metabolite ratios, such as N-acetyl-aspartate/creatine-phosphocreatine and N-acetyl-aspartate/choline, and declines in the hippocampal neuronal density have also been reported in patients with OCD [6]. Dysfunction in the frontobasal ganglia circuitry has been proposed in the pathophysiology of Parkinson's disease, a neurodegenerative disease, and a similar dysfunction has also been proposed for OCD [3,7,8]. In fact, some research has claimed a possible

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involvement of shared circuitry in the manifestation of both OCD and Parkinson's disease to explain the higher incidence of obsessive-compulsive symptoms in patients with Parkinson's disease [9,10]. However, the findings of a study by Harbishettar et al. did not support a relationship between OCD and Parkinson's disease [11].

Neurodegenerative diseases may cause ocular effects, such as a reduction in the retinal nerve fiber layer (RNFL) and the ganglion cell complex (GCC), and these can be detected by optical coherence tomography (OCT) [12]. Therefore, evaluation of OCT findings in patients with OCD may be important for understanding the controversial shared pathophysiology of OCD and Parkinson's disease, as both show retinal neuron degeneration. The RNFL contains axons, while GCC involves the bodies of ganglion cells; hence, the RNFL reduction may be the result of myelin loss in axons and glial cells [13]. OCT has been suggested as an effective way to diagnose axonal damage [14], and several studies have shown an association between retinal neuron degeneration and the severity of several neurodegenerative diseases, including multiple sclerosis (MS), Parkinson's disease, and Alzheimer's disease [15,16,17].

The first study to use OCT as a diagnostic tool for neuronal degeneration in psychiatric disorders revealed an RNFL reduction in patients with schizophrenia [18]. Another study found a relationship between abnormal OCT parameters and disease duration in patients with schizophrenia [19]. The levels of retinal dopamine, a chemical that plays a major role as a modulator in the retina, are also lower in patients with schizophrenia than in control subjects [20]. The presence of obsessive-compulsive symptomatology following high doses of stimulants and an improvement of these symptoms with antidopaminergic drugs suggest that dopamine also has an important involvement in the pathogenesis of OCD [21,22]. Dopamine irregularity plays a major role in psychosis, and dopamine is thought to regulate the relationship between the prefrontal cortex and the amygdala to mediate obsessive-compulsive symptoms. Therefore, dopamine irregularity could also conceivably lead to changes in the RNFL and GCC in patients with OCD, as observed in patients with schizophrenia [18,23].

Few studies have investigated the relationship between neurodegeneration in OCD and OCT findings. Neurodegeneration throughout the course of OCD suggests that OCT findings, such as RNFL and GCC decreases, may have therapeutic implications. The aim of this study was to examine the potential relationship between OCT findings and the clinical features of patients diagnosed with OCD according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria by comparing them with the findings in a healthy control group.

METHODS

Samples

The study included 42 consecutive subjects aged between 18–65 years who were recently diagnosed and/or had been followed up with a diagnosis of OCD based on the DSM-5 criteria. All subjects were recruited from Bakirkoy Training and Research Hospital Outpatient Clinic between January 2020 and April 2020, and diagnoses were obtained by means of the Structured Clinical Interview based on the DSM-IV axis I criteria [24]. A further 50 healthy subjects, matched with the patient group in terms of age and gender, were also included in the study as a control group. The subjects in the control group had no psychiatric disorders according to DSM-5 as determined by the Structured Clinical Interview non-patient edition [25]. Written informed consent was obtained from all subjects prior to enrollment. Individuals with cooperation problems or cognitive impairment as a result of mental retardation, neurological disease, or alcohol/drug use; those who had undergone electroconvulsive therapy in the last 6 months; and those with a history of psychosurgery or other brain surgery, head trauma, alcohol/drug addiction, psychotic symptoms, comorbidity, or any other psychiatric disease (for the patient group) or ophthalmologic disease (glaucoma, retinal disease, refraction disturbances) were excluded from the study. The study protocol was approved by the Ethics Committee of the Bakirkoy Dr. Sadi Konuk Training and Research Hospital (December 12nd, 2019, protocol number 2019-25-08).

The Sociodemographic Data Form, Beck Depression and Beck Anxiety Inventories were administered to both the study and control groups. Severity and types of symptoms in the OCD group were measured with Yale-Brown Obsessive Compulsive Scale (Y-BOCS). OCT assessments were performed by the Ophthalmology Department of the Bakırköy Dr. Sadi Konuk Research and Training Hospital. The RNFL and GCC volumes were measured and recorded with a spectral OCT instrument. Both groups were examined in the ophthalmology clinic, and visual acuity (best correct visual acuity, BCVA), intraocular pressure, slit lamp biomicroscopy, and fundus examinations were performed for all subjects. All patients and healthy controls included in the study had normal ophthalmologic examination results.

INSTRUMENTS

Sociodemographic Data Form: Sociodemographic data form was prepared by the researchers to assess the participants' sociodemographic and clinical characteristics. The form was completed by the researchers while interviewing the control and patient groups. This data form comprised questions about the participants' age, gender, marital status, education and employment status as well as personal and family history. Clinical data such as age of onset of disease, age of diagnose, age of the first treatment, number of hospitalizations, duration of the disease, duration without treatment and treatment were also included on the form.

Structured Clinical Interview for DSM-IV (SCID-I): SCID-I is a diagnostic tool which is used for determination of DSM-

IV Axis I disorders and the evaluation is performed by a professional interviewer. Consisting of 6 modules, the instrument was developed by First et al. and the validity and reliability of the Turkish version was confirmed by Ozkurkcugil under the name of the Structural Clinical Interview for DSM-IV Axis-I Disorders [26].

Yale-Brown Obsessive Compulsive Scale (Y-BOCS): The scale has been designed to evaluate the type and severity of symptoms in patients with OCD. YBOCS Symptom Checklist is used to generate a list of currently existing symptoms. Consisting of 19 items, the instrument is a semi-structured interview depending on the patient's report and clinical judgment of the interviewer. Originally developed by Goodman, Price and Rassmusen in 1989, Turkish reliability and validity has been evaluated by Karamustafalıoğlu et al in 1993 [27,28].

Beck Depression Inventory (BDI): The BDI is a self-report scale that measures physical, emotional, and cognitive indicators of depression. The maximum score is 63, with higher scores indicating more severe depression. The BDI was developed by Beck to determine the severity of depressive symptoms and validity and reliability studies for the Turkish form were conducted by Hisli et al. [29,30]

Beck Anxiety Inventory (BAI): The BAI is a self-report scale that measures the frequency of anxiety symptoms experienced by the individual. It was developed by Beck et al. and Turkish validity and reliability studies were conducted by Ulusoy et al. [31,32].

OCT Measurement:OCT images were taken and recorded from all the subjects in the patient and control groups using an Optovue RTVue Fourier domain OCT device (RTVue-100, 2007, version 3.0) in the Ophthalmology Polyclinic of Bakirkoy Dr. Sadi Konuk Training and Research Hospital. All tests were conducted by the same experienced OCT technician. The protocol consisted of 360˚ scanning, taking the optic disc as the center, with a 3.45mm diameter around the optic disc. The RNFL was evaluated with the rapid RNFL test.

Statistical Analyses

All statistical analyses were performed using SPSS version 22.0 software (Microsoft Co., Chicago, IL, USA). Descriptive statistical methods including mean, standard deviation, frequency and ratio values were used. The assumption of normality in the data was evaluated with the Kolmogorov–Smirnov test. A chi-square test and Fischer test when test conditions are not met were applied for qualitative independent variables between the OCD and control groups including the ratios of sex, occupational status, marital status and suicide attempt. Student's t test was was applied for quantitative independent data with normal distribution between the case and control groups, including GCC and RNFL values. The Mann-Whitney U test was used for quantitative independent variables with non-normal distribution between the case and control groups including age, duration of education, Beck Anxiety and Depression scores. The generalized estimating equations (GEE) method was used to compare the RNFL and GCC volumes between the patient and control groups. GEE is an established method of analyzing paired biological data (e.g., OCT data from a pair of eyes) and enables the use of data from both eyes while protecting against the conflation of statistical significance that can result from the use of paired biological data from the same subject (i.e., pair of eyes) [33]. Univariate and multivariate logistic regression served to determine the effect level of age, occupational status, GCC superior, GCC inferior, GCC mean and RNFL mean values in the differentiation of OCD participants from controls. The levels of the effect and cut-off values were examined using ROC curve analysis. Spearman's test was used to evaluate correlations between GCC mean value and age of onset, duration of the disease, duration of untreated disease, YBOC, Beck Anxiety and Beck Depression scores in the OCD group. A value of $p<0.05$ was considered statistically significant.

RESULTS

RNFL analysis and GCC scanning protocols were applied to map the optic nerve head of each eye. Figure 1 presents evaluation of retinal nerve fiber layer thickness with OCT.

The mean nerve fiber thickness value for all the eyes was automatically calculated in micrometers (μm) with this method (Figure 1).

Figure 2 presents evaluation of GCC with OCT.

The GCC scanning protocol was used to calculate the mean GCC value in mm^3 (Figure 2). Table 1 presents data comparing the sociodemographic characteristics and clinical variables of the groups. The Mann-Whitney U test, Student's t-test and chi-square test were used to compare the groups.

Age, gender, marital status, years of education distributions did not differ significantly between the OCD and healthy control groups ($p > 0.05$). The rate of employement was significantly lower in the OCD group than in the healthy control group ($p < 0.05$). Beck Anxiety score and Beck Depression score did not differ significantly between the OCD and healthy control groups ($p > 0.05$). In the OCD group; GCC superior, GCC inferior, GCC mean values were significantly lower than the healthy group. ($p < 0.05$). RNFL inferior, RNFL superior values did not differ significantly between the OCD and healthy groups ($p > 0.05$). The mean value of RNFL in the OCD group was significantly lower ($p < 0.05$) than the healthy group (Table 1).

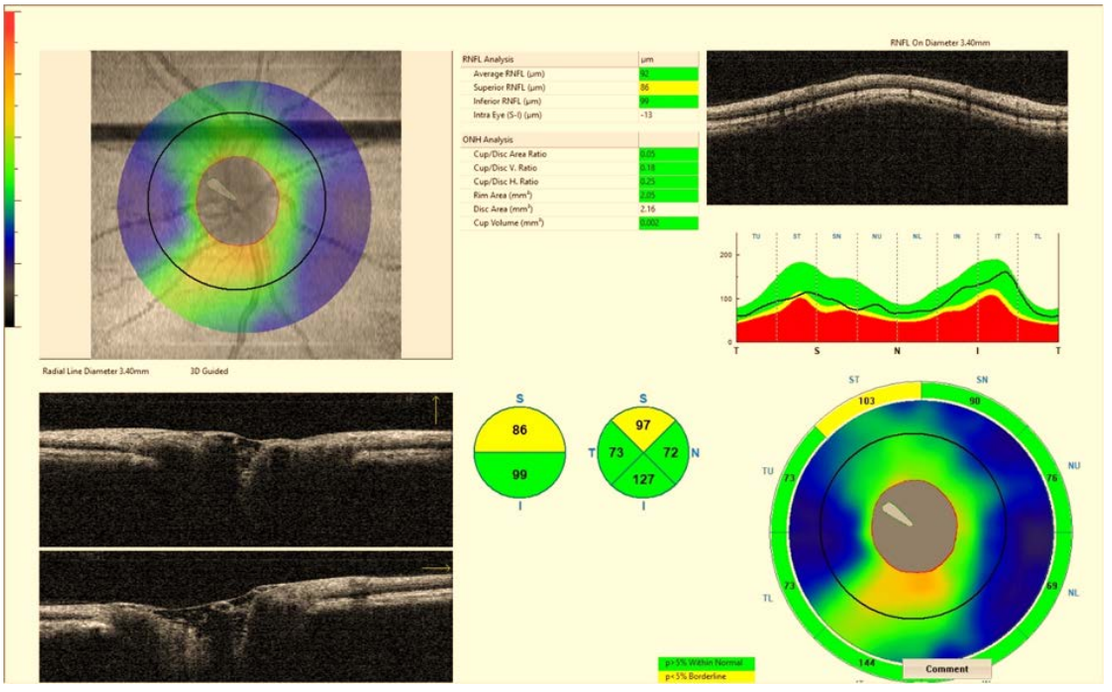

Figure 1. Evaluation of retinal nerve fiber layer thickness with OCT. Right and left eye RNFL thicknesses measurements were performed with the OCT device. Three measurements were performed for the RNFL measurement in each eye: Superior (S), Inferior (I) and mean.

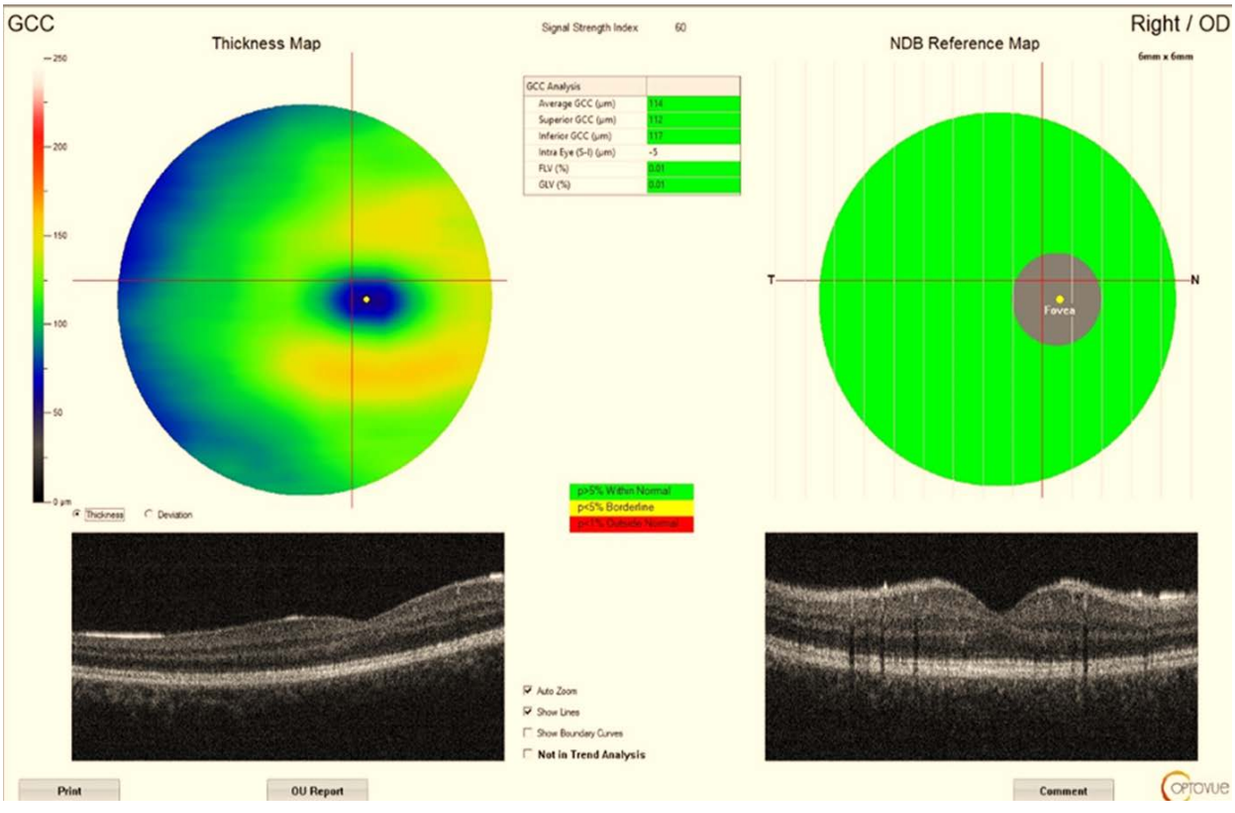

Figure 2. Evaluation of Ganglion Cell Complex with OCT. Right and left eye GCC volume measurements were performed with the OCT device. Three measurements were performed for the GCC measurement in each eye: Superior (S), Inferior (I) and mean. GCC: Ganglion Cell Complex.

Table 1. Comparison of Groups in Terms of Sociodemographic and Clinical Variables

		OCD				Healthy				p	
		mean±sd/n-%			Median	mean±sd n-%			Median		
Age		35.1	±	10.4	33.5	35.6	±	8.7	33.0	0.854	m
Sex	Female	27		64.3%		37		74.0%		0.313	X^2
	Male	15		35.7%		13		26.0%			
Duration of Education(years)		9.0	±	4.0	8.0	10.7	±	4.1	11.0	0.057	m
Marital Status	Married	28		66.7%		38		76.0%		0.448	X^2
	Single	12		28.6%		12		24.0%			
	Divorced/Widow	2		4.8%		0		0.0%			
Occupational Status	Present	20		47.6%		47		94.0%		**0.000**	X^2
	Absent	22		52.4%		3		6.0%			
Suicide Attempt	Present	2		4.8%		1		2.0%		0.590	X^2
	Absent	40		95.2%		49		98.0%			
Beck Anxiety		4.8	±	2.1	4.5	3.9	±	0.6	4.0	0.116	m
Beck Depression		4.4	±	1.7	4.0	3.8	±	0.7	4.0	0.052	m
GCC Superior		96.5	±	7.3	96.0	102.0	±	6.3	102.2	**0.000**	t
GCC İnferior		98.0	±	6.1	97.5	103.3	±	7.2	103.8	**0.000**	t
RNFL Superior		105.0	±	9.8	104.5	109.0	±	9.7	110.7	0.057	t
RNFL İnferior		98.6	±	8.7	99.0	101.5	±	6.0	102.0	0.057	t
GCC mean		97.2	±	6.4	96.3	102.6	±	6.6	103.5	**0.000**	t
RNFL mean		101.8	±	8.8	103.0	105.3	±	6.4	104.8	**0.032**	t

[m] Mann-whitney U test / [t] t test / [X^2]Chi-square test (Fischer test) sd:Standard Deviation n:Number of participants
GCC:Ganglion Cell Complex RNFL:Retinal Nerve Fiber Layer OCD:Obsessive Compulsive Disorder
Sociodemographic data and OCT variables for 42 OCD and 50 healthy controls were compared. p value of <0.05 was considered statistically significant and is shown in bold.

Table 2 presents data on disease characteristics in the OCD group.

The mean age at disease onset in the OCD group was 24.0±7.6 years. The mean age at diagnose was 26.5±7.9 years. Duration without treatment was 4.3±2.6 years. Mean YMRS score was 30.0±8.1 (Table 2). The medications are also shown in Table 2.

Binomial logistic regression analysis was applied to determine whether the differentiation of the groups was predicted by the significant variables obtained from the analyses (Occupational Status, GCC Superior, GCC İnferior, GCC mean, RNFL mean). Results are presented in Table 3.

Table 2. Clinic Variables of the OCD group

		Min-Max			Median	Mean±sd/n-%		
Obsession Type	Autogen obsession					21		50.0%
	Reactive obsession					21		50.0%
Age of Onset		10.0	-	40.0	22.0	24.0	±	7.6
Age of Diagnose		11.0	-	44.0	25.0	26.5	±	7.9
Age of the first Treatment		14.0	-	44.0	26.5	28.1	±	7.9
YBOC		20.0	-	55.0	29.0	30.0	±	8.1
Duration without Treatment (years)		0.0	-	8.0	5.0	4.3	±	2.6
Psychiatric Hospitalization	Present					4		9.5%
	Absent					38		90.5%
Duration of the disease (years)		1.0	-	38.0	9.5	11.0	±	8.4
Number of Hospitalization		1.0	-	1.0	1.0	1.0	±	0.0
Treatment	SSRI					3		7.1%
	SNRI					1		2.4%
	Antipsychotic					9		21.4%
	SSRI+Antipsychotic					1		2.4%
	SSRI+Antipsychotic+Anxiolytics					1		1.1%

Autogen:Religious, Sexual and Aggression obsessions Reactive obsession: Other obsessions Min:minimum Max:maximum YBOC:Yale Brown Obsession Compulsion Scale SSRI:Serotonin Selective Reuptake Inhibitor SNRI:Serotonin Noradrenaline Reuptake Inhibitor sd:Standard deviation n:number of participiants. Clinical data for 42 OCD patients.

When all independent variables were entered in the equation, it was determined that the probability value of the logistic regression model (2 Log) was 112.337. In addition, the value of the Nagelkerke R-square was 0.195, while the Cox & Snell R-square was 0.146. The model in this step was found to significantly explain the probability of being included in the differentiation of groups (X2:14.505, p<0.05). In the univariate model, significant effect of occupational status, GCC superior, GCC inferior, GCC mean, RNFL mean values was observed in differentiation of OCD and healthy control group (p <0.05). Significant-independent effect of GCC mean value was observed in the multivariate reduced model in differentiation of OCD and healthy control group (p <0.05) (Table 3).

Figure 3 presents ROC curve analysis results for GCC cut-off values in the differentiation of OCD patients from healthy controls

Table 3. Regression Analysis for Differentiating OCD and Healthy Groups

	Univariate Model						Multivariate Model				
	OR	%95			p		OR	%95			p
Occupational Status	17.233	4.627	-	64.182	**0.000**						
GCC Superior	0.888	0.830	-	0.951	**0.001**						
GCC İnferior	0.887	0.827	-	0.951	**0.001**						
GCC mean	0.882	0.821	-	0.947	**0.001**		0.887	0.820	-	0.958	**0.002**
RNFL mean	0.940	0.886	-	0.996	**0.037**						
Age	0.994	0.951	-	1.038	0.781						

Binomial Logistic Regression (Forward LR),p value of <0.05 was considered statistically significant and is shown in bold. GCC:Ganglion Cell Complex RNFL:Retinal Nerve Fiber Layer OR:Odds Ratio

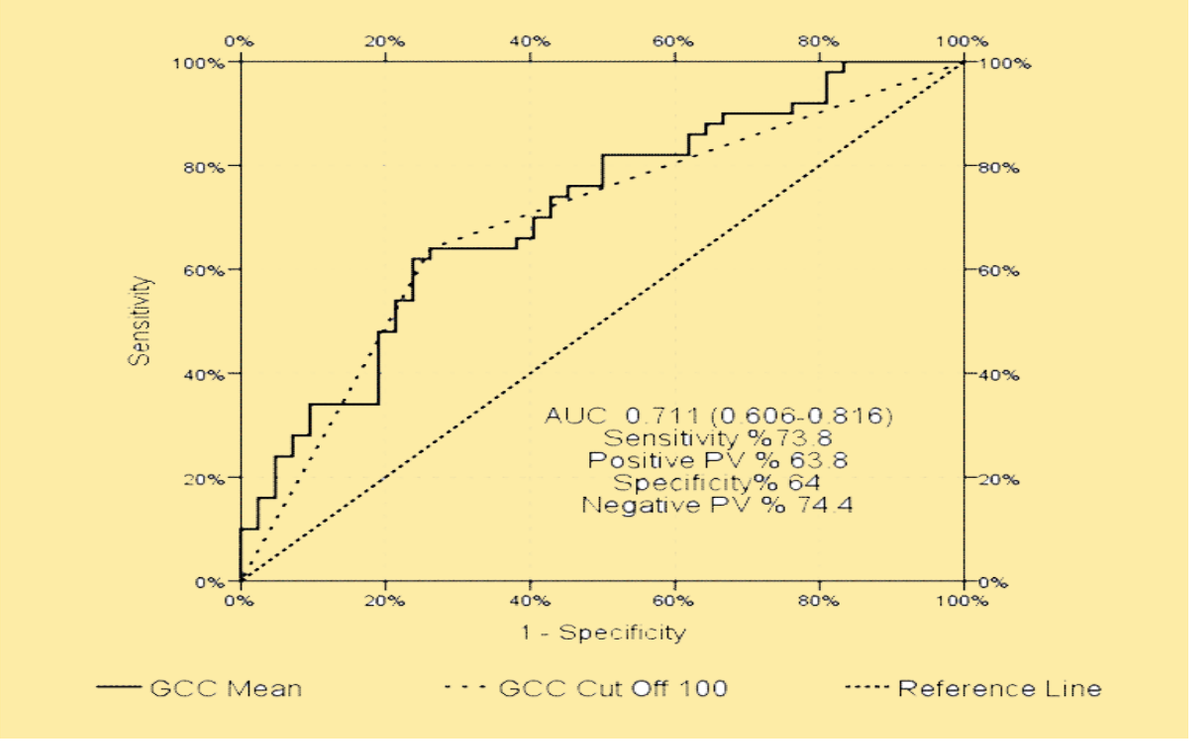

Figure 3. ROC Analysis for GCC mean. Significant efficacy of GCC mean value [sub-curve area 0.711 (0.606-0.816)] was observed in the differentiation of OCD and healthy control group. The GCC cut-off value of 100 mm³ was significant for the differentiation of the patient and control groups [AUC 0.711 (0.606-0.816)], with a sensitivity of 73.8%, a specificity of 64.0%, a positive predictive value (PPV) of 63.8%, and a negative predictive value (NPV) of 74.4%. GCC: Ganglion Cell Complex AUC:Area Under Curve PV:Predictive Value.

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predictive value (PPV) of 63.8%, and a negative predictive value (NPV) of 74.4% (Figure 3).

Spearman's correlation analysis was used to investigate the relationship between clinic variables and GCC mean value in the OCD group. Findings are presented in Table 4.

Significant positive correlation was observed between the age of onset of OCD and GCC mean value ($p < 0.05$). A significant negative correlation was observed between the duration of untreated disease and the GCC mean value ($p < 0.05$). No significant correlation was observed between duration of untreated disease, duration of disease, YBOC, Beck Anxiety, Beck Depression scores and GCC mean value ($p > 0.05$) (Table 4).

Table 4. Correlation Analysis Between Clinic Variables and GCC global value

		OCD Age of Onset	Duration of Untreated Disese	Duration of Disease	YBOC	Beck Anxiety	Beck Depression
GCC mean value	r	0.342	-0.346	-0.007	-0.172	-0.007	-0.060
	p	**0.026**	**0.025**	0.966	0.276	0.945	0.569

Spearman Correlation
YBOC:Yale Brown Obsession Compulsion Scale Score GCC:Ganglion Cell Complex OCD:Obsessive Compulsive Disorder p value of <0.05 was considered statistically significant and is shown in bold.

DISCUSSION

The results of this study demonstrated that the mean RNFL and GCC were thinner in patients with OCD than in healthy control subjects. In addition, measurement of the mean GCC volume showed significant and independent efficacy in differentiating the OCD group from the control group. These results differ in some respects from previous studies regarding the association between the clinical features of OCT and the RNFL and GCC volume.

For example, Özen et al. found that the GCC was thinner in patients with OCD than in control subjects. In our study, a statistically significant decrease was also observed in the thickness of the superior, inferior, and global GCC in the OCD group [34]. Özen et al. also reported a decrease in all parts of the RNFL, although only the difference in the mean left temporo-superior RNFL was statistically significant. That study also found a much sharper decrease in the GCC volume than in the RNFL [34]. By contrast, Polat et al. reported no decrease in the RNFL of patients with OCD [35]. The results of our study also showed that the mean GCC volume had a significant and independent efficacy in differentiating the OCD from the control group. Moreover, we did not find a significant difference between the two groups in terms of RNFL expect RNFL mean. The RNFL shows a similarity to the substantia grisea in the brain, and the changes in its thickness depend only on axonal damage. For this reason, RNFL damage assessment is only possible after the ganglion cell damage reaches 50 percent [19]. In other words, our study supports the view that a significant decrease in RNFL can only be noticed when the disease progresses.

Inflammation may be another reason for the different findings in RNFL and GCC volumes. An autopsy study by Green et al. revealed prominent gliosis and inflammation surrounding the vessels of the inner retina, and these changes were shown to impact OCT findings, since the retinal vasculature sits embedded in the RNFL in MS patients [36]. Ascaso et al. also suggested that the neuroinflammation occurring during illness episodes increases the retinal thickness and masks the decrease in RNFL in schizophrenia patients during acute episodes [37]. In the present study, a cut-off value of 100 mm^3 was calculated for the mean GCC to distinguish OCD patients from healthy control subjects, and this provided a 73.8% sensitivity and 64% specificity. Although this specificity is low, our results support the idea that neurodegeneration in OCD starts in the GCC, which forms the neuronal cell bodies, and then gradually progresses to axonal degeneration. Our results indicate that neuronal degeneration in OCD is characterized by a thinning of the GCC and that OCT findings may be used as markers in the follow-up of patients with OCD.

Previous research has documented that the duration of schizophrenia correlates with RNFL thinning [19]. For example, Özen et al. found a statistically significant relationship between the duration of OCD and the extent of RNFL loss [34]. By contrast, in our study, and in agreement with previous findings by Polat et al., no significant relationship was evident between the duration of the disease and the changes in the RNFL or GCC [35]. This discrepancy could be attributed to the older mean age of our patients with OCD than the patients investigated by Özen et al. [34]. Although our groups were age-matched, age may persist as a confounding variable because of its relationship with RNFL thinning [38].

Current evidence shows that patients with Bipolar Disorder Type 1 (BPD1) undergo more progressive brain-aging changes, such as loss of gray matter density, when compared with the normal population [38]. The difference in the subtypes of obsessions and compulsions may be related to gray matter loss, as well as a potential independent RNFL reduction. For example, Mataix-Cols et al. found that patients with controlling compulsions demonstrated greater activation in the right putamen/globus pallidus, right thalamus, and dorsal cortical areas when compared with controls. By contrast, when compared with controls, patients with washing compulsions exhibited significantly greater activation during symptom provocation in the bilateral ventromedial prefrontal regions and the right caudate nucleus, which are areas also known to be responsible for emotional processes [39]. Özen et al. and Polat et al. did not use the Yale-Brown Obsessive Compulsive symptom checklist, and our study sample size was smaller than in those previous studies. Therefore, studies with wider participation may be needed to investigate RNFL and GCC thickness according to the YBOC obsession types [34,35].

Cell culture and animal research data indicate that

neuroprotectivity may be elicited by the use of selective serotonin reuptake inhibitors (SSRIs) [40,41]. In our study, most patients were receiving SSRI treatment, and we found that the duration of the untreated disease showed a significant negative correlation with the thicknesses of the GCC and RNFL. Güçlü et al. also reported a possible relation between SSRIs and decreased retinal GCC volume and RNFL thickness [42]. However, the observed differences may have arisen because the sample in that study consisted of different patients using SSRIs, and not just patients with OCD. In addition, patients who were receiving drug combinations, including SSRIs + antipsychotics, serotonin and noradrenalin reuptake inhibitors (SNRIs), and SSRIs + antipsychotics + anxiolytics, were also included in our study. Our results strongly suggest that neurodegeneration progresses faster in OCD patients who remain untreated.

This study had certain limitations. One limitation is that we recruited OCD patients who were undergoing pharmacotherapy. Another limitation is that we did not compare the OCD and control groups in terms of smoking habit. A third limitation is that we excluded "at risk" subjects (i.e., those with a first-degree relative diagnosed with a psychiatric disorder) from the control group.

CONCLUSION

Overall, our results suggest that neurodegeneration may manifest itself particularly as changes in the GCC and RNFL volumes and that treatment for OCD may be neuroprotective. These findings can be considered important, as they have implications for the neurobiology of OCD, its treatment considerations, and the course of the disease. Further studies using OCT are needed to compare patients with OCD at early and later stages to acquire a better understanding of the disease's effects.

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REFERENCES

[1] Hollander E. Obsessive-compulsive disorder and spectrum across the life span. Int J Psychiatry Clin Pract 2005;9(2):79-86. https://doi.org/10.1080/136.515.0051 0018347.

[2] Robinson D, Wu H, Munne RA, Ashtari M, Alvir JM, Lerner G, et al. Reduced caudate nucleus volume in obsessive-compulsive disorder. Arch Gen Psychiatry 1995;52:393-8. https://doi.org/10.1001/ archpsyc.1995.039.50170067009.

[3] Saxena S, Brody AL, Schwartz JM, Baxter LR. Neuroimaging and frontal-subcortical circuitry in obsessive-compulsive disorder. Br J Psychiatry 1998;173:26-37. https://doi. org/10.1192/S000.712.5000297870.

[4] Behar D, Rapoport JL, Berg CJ, Denckla MB, Mann L, Cox C, et al. Computerized tomography and neuropsychological test measures in adolescents with obsessive-compulsive disorder. Am J Psychiatry 1984;141:363-9. https://doi. org/10.1176/ajp.141.3.363.

[5] Ebert D, Speck O, Konig A, Berger M, Hennig J, Hohagen F. 1H-magnetic resonance spectroscopy in obsessive-compulsive disorder: evidence for neuronal loss in the cingulate gyrus and the right striatum. Psychiatry Research 1997;74:173-176. https://doi.org/10.1016/ S0925-4927(97)00016-4.

[6] Atmaca M, Yıldırım H, Ozdemir H, Koc M, Ozler S, Tezcan E. Neurochemistry of the hippocampus in patients with obsessive-compulsive disorder. Psychiatry and Clinical Neurosciences 2009;63:486-490. https://doi. org/10.1111/j.1440-1819.2009.01993.x.

[7] Tomer R, Levin BE, Weiner WJ. Obsessive compulsive symptoms and motor asymmetries in parkinson's disease. Neuropsychiatry, Neuropsychology, Behavioral Neurology 1993;6:26-30.

[8] Rauch SL, Savage CR. Neuroimaging and neuropsychology of the striatum: bridging basic science and clinical practice. Psychiatry Clinics of North America 1997;20:741-68. https://doi.org/10.1016/S0193-953X(05)70343-9.

[9] Alegret M, Junque C, Valldeoriola F, Vendrell P, Marti MJ, Tolosa E. Obsessive-compulsive symptoms in parkinson's disease. Journal of Neurology Neurosurgery and Psychiatry 2001;1:58-60. http://dx.doi.org/10.1136/ jnnp.70.3.394.

[10] Lees AJ. The neurobehavioral abnormalities in parkinson's disease and their relationship to psychomotor retardation and obsessional compulsive disorders. Behavioural Neurology 1989;2:1-11.

[11] Harbishettar V, Pal PK, Reddy YJ, Thennarasu K. Is there a relationship between parkinson's disease and obsessive-compulsive disorder?. Parkinsonism & related disorders 2005;11: 85-88.

[12] Galetta KM, Calabresi PA, Frohman EM, Balcer LJ. Optical coherence tomography (oct): imaging the visual pathway as a model for neurodegeneration. Neurotherapeutics 2011; 8:117-132. https://doi. org/10.1007/s13311.010.0005-1.

[13] Parver LM. Temperature modulating action of choroidal blood flow. Eye 1991;5:181-5. https://doi.org/10.1038/ eye.1991.32.

[14] Schönfeldt-Lecuona C, Kregel T, Schmidt A, Pinkhardt EH, Lauda F, Kassubek J, et al. From imaging the brain to imaging the retina: optical coherence tomography (oct) in schizophrenia. Schizophr Bull 2015;42:9-14. https:// doi.org/10.1093/schbul/sbv073.

[15] Petzold A, de Boer JF, Schippling S, Vermersch P, Kardon R, Green A, et al. Optical coherence tomography in multiple sclerosis: a systematic review and meta-analysis. Lancet Neurol 2010;9:921-932. https://doi. org/10.1016/s1474-4422(10)70168-x.

[16] Inzelberg R, Ramirez JA, Nisipeanu P, Ophir A. Retinal

nerve fiber layer thinning in parkinson disease. Vision Res 2004;44:2793-2797. https://doi.org/10.1016/j.visres.2004.06.009.

[17] Lu Y, Li Z, Zhang X, Ming B, Jia J, Wang R, et al. Retinal nerve fiber layer structure abnormalties in early alzheimer's disease: evidence in optical coherence tomography. Neurosci Lett 2010;480:69-72. https://doi.org/10.1016/j.neulet.2010.06.006.

[18] Ascaso FJ, Cabezón L, Quintanilla MÁ, Galve LG, López-Antón R, Cristóbal JA, et al. Retinal nerve fiber layer thickness measured by optical coherence tomography in patients with schizophrenia: a short report. The European Journal of Psychiatry 2010;24:227-235.

[19] Lee WW, Tajunisah I, Sharmilla K, Peyman M, Subrayan V. Retinal nerve fiber layer structure abnormalities in schizophrenia and its relationship to disease state: evidence from optical coherence tomography. Invest Ophthalmol Vis Sci 2013;54:7785-7792. https://doi.org/10.1167/iovs.13-12534.

[20] Djamgoz MBA, Hankins MW, Hirano J, Archer SN. Neurobiology of retinal dopamine in relation to degenerative states of the tissue. Vision Res 1997;37:3509–3529. https://doi.org/10.1016/s0042-6989(97)00129-6.

[21] Coskun M. Methylphenidate induced obsessive-compulsive symptoms treated with sertraline. Bulletin of Clinical Psychopharmacology 2011;21:275 (Turkish). doi: 10.5455/bcp.201.106.20021611.

[22] Karslıoğlu EH, Yüksel N. Obsesif kompulsif bozukluğun nörobiyolojisi. Klinik Psikiyatri 2007;10:3-13 (Turkish).

[23] Denys D, Zohar J, Westenberg HG. The role of dopamine in obsessive compulsive disorder: preclinical and clinical evidence. The Journal of Clinical Psychiatry 2004;65:11-17.

[24] First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM IV-TR axis I disorders (SCID) research version. New York:New York State Psychiatric Institute;2002.

[25] First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM IV-TR axis I disorders, research version, non-patient edition (SCID-1/ NP). New York: New York State Psychiatric Institute, Biometric Research;2002.

[26] Ozkürkçügil A, Aydemir Ö, Yıldız MK, Danacı E, Köroğlu E. Structured clinical interview for DSM-IV axis I disorders-clinical version (SCID-CV) in Turkish: study of reliability. İlaç ve Tedavi Dergisi 1999;12:233-236 (Turkish).

[27] Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, et al. The yale-brown obsessive compulsive scale development, use, and reliability. Arch Gen Psychiat 1989;46:1006-11. https://doi.org/10.1001/archpsyc.1989.018.10110048007.

[28] Karamustafalıoğlu O, Üçışık AM, Ulusoy M, Erkmen H. A reliability and validity study of the yale-brown obsessive compulsive scale in: 29. National Psychiatry Congress Program and Abstract Book (Turkish). Bursa: Savaş Ofset 86; 1999.

[29] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71. https://doi.org/10.1001/archpsyc.1961.017.10120031004.

[30] Hisli N. A reliability and validity study of beck depression Inventory in a university student sample. Türk Psikoloji Dergisi 1989;7:3-13 (Turkish).

[31] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. Journal of Consulting and Clinical Psychology 1988;56:893-897. https://doi.org/10.1037//0022-006x.56.6.893.

[32] Ulusoy M, Sahin NH, Erkmen H. Turkish version of the beck anxiety inventory: psychometric properties. Journal of Cognitive Psychotherapy 1998;12:163-172. https://doi.org/10.1200/JCO.2011.39.8123.

[33] Hanley JA, Negassa A, Edwardes MD, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. Am J Epidemiol 2003;157:364-75. https://doi.org/10.1093/aje/kwf215.

[34] Ozen ME, Kalenderoglu Y, Karadağ AS, Orum MH. Comparison of optic coherence tomography results in patients diagnosed with ocd: findings in favor of neurodegeneration. Anatolian Journal of Psychiatry 2019;20:166-175. doi: 10.5455/apd.301482

[35] Polat S, Gediz BS, Ercan AC, Kaim M, Hocaoglu C. The place of optical coherence tomography in patients with obsessive compulsive disorder. Eurasian Journal of Medicine 2019;51:237. https://doi.org/10.5152/eurasianjmed.2019.18306.

[36] Green AJ, McQuaid S, Hauser SL, Allen IV, Lyness R. Ocular pathology in multiple sclerosis: retinal atrophy and inflammation irrespective of disease duration. Brain 2010;133:1591-601. https://doi.org/10.1093/brain/awq080.

[37] Ascaso FJ, Rodriguez-Jimenez R, Cabezón L, López-Antón R, Santabárbara J, De la Cámara C, et al. Retinal nerve fiber layer and macular thickness in patients with schizophrenia: influence of recent illness episodes. Psychiatry Res 2015;229:230-6. https://doi.org/10.1016/j.psychres.2015.07.028.

[38] Yatham LN, Kapczinski F, Andreazza AC, Trevor Young L, Lam RW, Kauer-Sant'anna M. Accelerated age-related decrease in brain-derived neurotrophic factor levels in bipolar disorder. Int J Neuropsychopharmacol 2009;12:137-9. https://doi.org/10.1017/s146.114.5708009449.

[39] Mataix-Cols D, Wooderson S, Lawrence N, Branner MJ, Speckens A, Phillips ML. Distinct neural correlates of washing, checking, and hoarding symptom dimensions in obsessive compulsive disorder. Arch Gen Psychiatry 2004;61:564-76. https://doi.org/10.1001/archpsyc.61.6.564.

[40] Taguchi N, Nakayama S, Tanaka M. Fluoxetine has neuroprotective effects after cardiac arrest and cardiopulmonary resuscitation in mouse. Resuscitation 2012;83:652-6. https://doi.org/10.1016/j.resuscitation.2011.11.004.

[41] Steiner JP, Bachani M, Wolfson-Stofko B, Lee MH,

Wang T, Li G, et al. Interaction of paroxetine with mitochondrial proteins mediates neuroprotection. Neurotherapeutics 2015;12:200-16. https://doi.org/10.1007/s13311.014.0315-9.

[42] Guclu H, Gorgulu Y, Gurlu VP, Kose Cinar R, Ozal SA, Çaliyurt O. Effects of selective serotonin reuptake inhibitors on macular ganglion cell complex thickness and peripapillary retinal nerve fiber layer thickness. Curr Eye Res 2018;43:547-552. https://doi.org/10.1080/02713.683.2017.1420198.