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Examination of the Corpus Callosum from Magnetic Resonance Images of Patients with Parkinson's Disease

Parkinson Hastalığı Olan Hastaların Manyetik Rezonans Görüntülerinden Korpus Kallozumun İncelenmesi

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ABSTRACT

Aim: In recent years, studies investigating white matter involvement, which is considered the cause of sensory symptoms that appear earlier than motor symptoms in Parkinson's disease, have increased. This study aims to investigate the involvement of the corpus callosum, the largest white matter structure connecting the two hemispheres, in Parkinson's disease, taking into account age and sex differences.

Materials and Methods: Our study were retrospectively compared the measurements of corpus callosum length, width, and angle on midsagittal magnetic resonance images from 120 controls without any diagnosis affecting the corpus callosum and from 120 patients diagnosed with Parkinson's disease.

Results: The height of the corpus callosum, the distance from the anterior tip to the top, and the distance from the anterointernal tip to the vertex increased, and the genu and rostrum width and the ratio of corpus callosum width to height decreased significantly in Parkinson's disease patients ($p<0.05$). Based on the angular measurements, it was determined that the mean value of Angle 2 decreased in patients with Parkinson's disease, while the values of Angle 4 and Angle 5 increased significantly ($p<0.05$).

Conclusion: It appears that there are few studies examining the involvement of the corpus callosum in Parkinson's disease, and to the best of our knowledge, no studies have evaluated the known angle parameters. Therefore, it is believed that research in this area may provide a novel perspective for clinicians and surgeons.

Keywords: Corpus callosum, magnetic resonance images, Parkinson's disease, white matter

ÖZ

Amaç: Son yıllarda, Parkinson hastalığında motor semptomlardan daha erken ortaya çıkan duyusal semptomların nedeni olarak kabul edilen beyaz cevher tutulumunu araştıran çalışmalar artış göstermiştir. Bu çalışma, iki beyin yarımküresini birbirine bağlayan en büyük beyaz cevher yapısı olan korpus kallozumun Parkinson hastalığındaki tutulumunu, yaş ve cinsiyet farklılıklarını da dikkate alarak incelemeyi amaçlamaktadır.

Gereç ve Yöntem: Çalışmamızda, korpus kallozumu etkileyen herhangi bir tanısı olmayan 120 kontrol grubuna ait ve Parkinson hastalığı tanısı konmuş 120 hastaya ait mid-sagittal manyetik rezonans görüntülerinde korpus kallozumun uzunluk, genişlik ve açı ölçümleri geriye dönük olarak karşılaştırıldı.

Bulgular: Parkinson hastalarında, korpus kallozumun yüksekliği, ön uçtan tepeye olan mesafe ve anterointernal uçtan tepeye olan mesafe arttı; genu ve rostrum genişliği ile korpus kallozum genişliğinin yüksekliğe oranı anlamlı düzeyde azaldı ($p<0,05$). Açısal değerlere bakıldığında, Parkinson hastalarında, Açı 2 ortalama değerinin azaldığı, Açı 4 ve Açı 5 değerlerinin ise anlamlı şekilde arttığı belirlendi ($p<0,05$).

Sonuç: Parkinson hastalığında korpus kallozum tutulumunu inceleyen az sayıda çalışma bulunmaktadır ve bildiğimiz kadarıyla açı değerlerin değerlendirildiği herhangi bir çalışma bulunmamaktadır. Bu nedenle, bu alanda yapılacak araştırmaların klinisyenler ve cerrahlar için yeni bir bakış açısı sağlayabileceği düşünülmektedir.

Anahtar Kelimeler: Korpus kallozum, manyetik rezonans görüntüleme, Parkinson hastalığı, beyaz cevher

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INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterized by a decrease or complete loss of dopamine release[1]. While gray matter structures in the brain are emphasized in the pathogenesis of PD, recent studies have revealed their effects on white matter structures and increased the tendency to investigate this subject.

Many studies using various techniques have demonstrated that the corpus callosum, the largest white matter structure facilitating the transfer and integration of lateralized cognitive, motor, and sensory information between the cortices, is affected in PD[2-5]. Some studies indicate that these effects may manifest much earlier than changes in gray matter, underscoring their significance for early-stage diagnosis[6,7].

The aim of this study is to investigate the changes in width, length, and angle that occur in the corpus callosum, taking into account measurement parameters that have not been previously examined, through magnetic resonance images (MRI).

MATERIALS AND METHODS

Study Population

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Tekirdağ Namık Kemal University (decision no: 2021.74.03.14, date: 30.03.2021). In this study, images archived in the hospital's picture archiving and communication system were retrospectively reviewed. Ethical approval was obtained, and the ethics committee stated that informed consent was not required due to the retrospective nature of the study. The data obtained from the PD group and the control group were analyzed by stratified sampling method, grouped by age and gender. A total of 500 MRI images from patients with PD were available as the study population. Based on the calculations, considering the small effect size, a 95% confidence interval, a 5% margin of error, and the sample sizes in other studies, the sample size was determined to be 120 MRI images from the PD group, obtained between 2018 and 2021 from patients without any other diagnosis affecting the corpus callosum, and 120 MRI images from the control group.

MRI images, including T1 and T2 sequences, were obtained in the cranial sagittal plane using a 1.5 Tesla MRI machine (Canon Vantage Elan or Philips Intera; Philips Medical Systems) and an eight-channel head coil. The images had a slice thickness of 5 mm and were analyzed using the programs OrDICOM 1.0 and Weasis 3.7.1.

The demographic data and group distributions of the participants are presented in Table 1.

Corpus Callosum Measurement Parameters

The corpus callosum is divided into four parts: rostrum, genu, truncus, and splenium. Measurements of length, height, width, and angle were taken for both groups using MRI images from the midsagittal section. Length, height, and width measurements are given in mm, while angle measurements are in degrees. All measurement sites are shown in Figure 1.

Statistical Analysis

The data were analyzed using IBM SPSS 24.0 software (Armonk, New York, USA), with a significance value of $p<0.05$. To compare changes across different age groups, the data were divided into six groups: 30-40 years (Group I), 41-50 years (Group II), 51-60 years (Group III), 61-70 years (Group IV), 71-80 years (Group V), and 81 years and above (Group VI).

RESULTS

Corpus Callosum Metric Measurement Results

The mean values of all morphometric measurements for both groups are presented in Table 2.

The averages of corpus callosum length (CCL), corpus callosum height (CCH), cerebrum length (CL), distance between the corpus callosum front end to vertex distance (FV), and distance between the corpus callosum anterointernal tip to vertex distance (AIV) were found to be greater in men than in women ($p<0.05$).

Analysis of the group of individuals diagnosed with PD by sex revealed statistically significant differences in CCL ($p=0.007$), CCH ($p=0.008$), rostrum width (RW) ($p=0.012$), and CL ($p<0.001$). The averages of the other parameters did not differ significantly by sex. As a result of the data analysis based on age groups, it was observed that the average values of corpus callosum width (CCW), genu width (GW), splenium width (SW), RW, and trunk width maximum (TW_{max}) decreased as the age of patients with Parkinson's disease increased, while the average values of CCH, FV, and AIV increased.

Table 1. Demographic distributions and group data

	PD group	Control group	p-value
Female/male (%)	55/65 (45.8%/54.2%)	81/39 (67.5%/32.5%)	0.001
Age (mean ± SD)	68.82±10.0	57.91±12.4	0.000

PD: Parkinson's disease, SD: Standard deviation

in patients with PD, especially those aged 81 years and older, CCW, GW, SW, and TW_{max} showed a significantly greater decrease compared to controls ($p<0.05$). However, AIV was significantly higher in patients with PD, aged 81 years and older. In patients with PD, it has been observed that these significant changes begin to become noticeable between the ages of 51 and 60 and accelerate after the age of 81. The ratio of CCW to CCH was also significantly lower in the PD group ($p=0.001$).

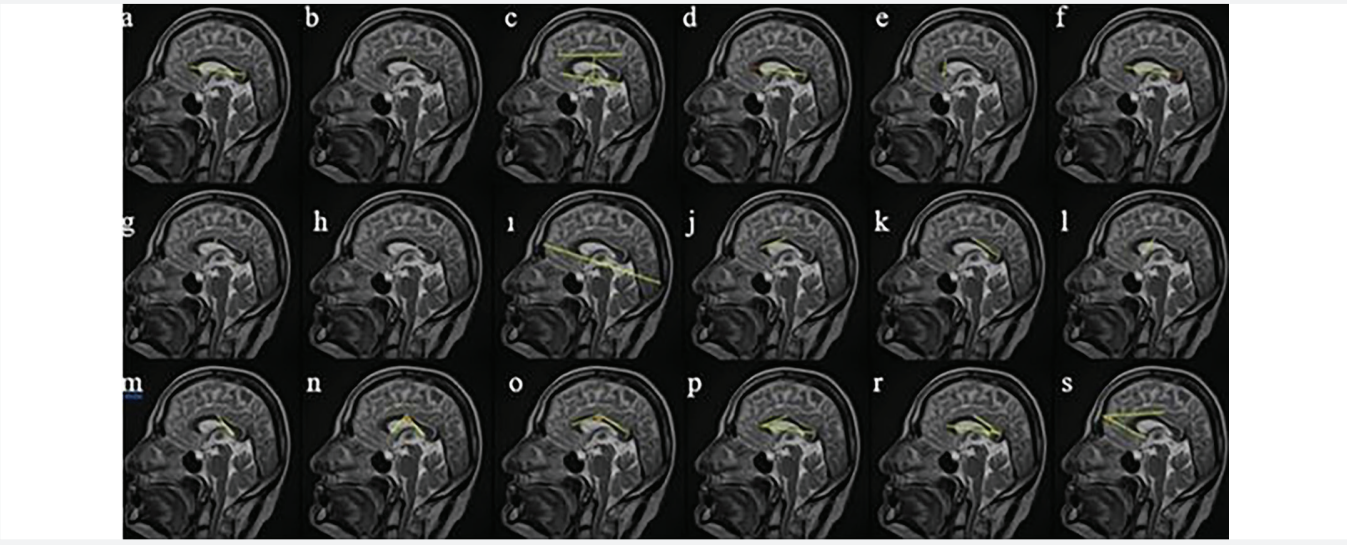

Figure 1. Corpus callosum measurements

a. Corpus callosum length (CCL), b. Corpus callosum width (CCW), c. Corpus callosum height (CCH), d. Genu width (GW), e. Rostrum width (RW), f. Splenium width (SW), g. Truncus maximum width (TW_{max}), h. Truncus minimum width (TW_{min}), i. Cerebrum length (CL), j. Front-end to vertex distance (FV), k. Posterior-end to vertex distance (PV), l. Anterointernal tip-to-vertex distance (AIV), m. Posterior inner tip-to-vertex distance (PIV), n. Angle between AIV and PIV (Angle 1), o. Angle between FV and PV (Angle 2), p. Angle between FV and CCU (Angle 3), r. Angle between AV and CCL (Angle 4), s. The angle between the line passing through the lower edge of the commissura anterior and genu and the tangent line passing over the anterior part of the corpus callosum (Angle 5)

Table 2. Comparison of average corpus callosum length across groups and by sex (mm)

	Control group			PD group			
	Female Mean ± SD	Male Mean ± SD	Total Mean ± SD	Female Mean ± SD	Male Mean ± SD	Total Mean ± SD	p*
CCL	68.3±4.2	69.8±4.5	68.8±4.3	67.8±4.2	70.1±4.7	69.1±4.6	0.654
CCW	4.6±0.9	4.3±0.7	4.5±0.9	4.3±0.9	4.6±1.0	4.5±1.0	0.534
CCH	24.0±2.9	24.9±2.9	24.3±2.9	25.3±3.3	27.1±3.7	26.3±3.6	0.000
GW	9.0±1.9	8.0±1.4	8.7±1.8	7.5±1.6	8.1±2.0	7.8±1.8	0.000
RW	4.9±1.1	4.7±1.4	4.8±1.2	3.8±1.2	4.4±1.0	4.1±1.1	0.000
SW	9.8±1.8	9.8±1.7	9.8±1.8	9.1±1.6	9.6±1.5	9.4±1.6	0.059
TW_{max}	5.1±1.0	4.7±0.7	4.9±1.0	4.7±0.9	5.0±0.9	4.9±0.9	0.825
TW_{min}	2.8±1.0	2.6±0.9	2.8±0.9	2.7±1.0	2.8±1.1	2.7±1.0	0.877
CL	153.8±7.3	160.3±7.2	155.9±7.9	152.2±6.4	159.4±6.7	156.1±7.4	0.886
FV	36.3±3.7	37.7±5.1	36.8±4.3	38.7±4.8	40.2±4.6	39.5±4.7	0.000
PV	39.8±4.4	40.0±4.6	40.6±5.1	38.2±3.8	39.6±4.4	39.0±4.2	0.060
AIV	29.3±3.9	31.0±4.5	29.9±4.1	32.5±4.2	33.3±4.2	32.9±4.2	0.000
PIV	34.2±3.6	34.7±4.4	34.4±3.9	33.1±3.6	34.6±4.5	33.9±4.1	0.429

*: Independent sample t-test $p<0.05$, SD: Standard deviation, CCL: Corpus callosum length, CCW: Corpus callosum width, CCH: Corpus callosum height, GW: Genu width, RW: Rostrum width, SW: Splenium width, TW_{max}: Trunk width maximum, TW_{min}: Trunk width minimum, CL: Cerebrum length, FV: Front end to vertex distance, PV: Posterior end to vertex distance, AIV: Anterointernal tip to vertex distance, PIV: Posterointernal tip to vertex distance

Corpus Callosum Angle Measurement Results

All the measurement results are presented in Table 3.

After comparing the average angles across different age groups, significant differences were found in Angle 1, Angle 2, and Angle 4 between the PD group and the control group, particularly in the 30-40 age group. Further analysis within the PD group showed statistically significant differences in Angle 1, angle 2, and Angle 5 values across different age groups ($p<0.05$). Specifically, Angle 2 decreases with age in patients with PD, while Angle 5 increases with age.

According to the analysis of the data set, there were weak negative correlations between age and SW (r=-0.263) and between age and TW_{min} (r=-0.216), and moderate negative correlations between age and CCW (r=-0.352), GW (r=0.568), RW (r=-0.347), and TW_{max} (r=-0.394). Additionally, weak positive relationships were detected between age and CCH (r=0.289), FV (r=0.205), Angle 4 (r=0.280), and Angle 5 (r=0.266). In the PD group, there was a weak negative correlation between age and Angle 2 (r=-0.197), but a weak positive correlation between age and Angle 4 (r=0.207) and Angle 5 (r=0.250). It is important to note that these correlations were not observed in the control group.

In the PD group, certain length measurements showed different correlation results compared to those in the control group. Specifically, there was a weak negative correlation between GW and CCH (r=-0.269, p=0.003). Moreover, moderate positive correlations were observed between CCH and RW (r=0.416, $p<0.001$) as well as between CCH and CL (r=0.310, p=0.001). Additionally, a weak positive relationship was found between CL and TW_{max} (r=0.187, p=0.041).

DISCUSSION

In PD, Lewy bodies affect gray matter structures and damage white matter connections, leading to non-motor symptoms such as cognitive impairment and depression[8]. Investigating changes in white matter fiber tracts may provide a better understanding of the underlying mechanism of PD. Our study is one of the most comprehensive studies to measure a wide range of parameters of the corpus callosum in MRI images of patients diagnosed with PD, including parameters that have not been previously evaluated.

Our research shows that women have smaller CCL and CL values than men, consistent with the findings of Mohammadi et al.[9] ($p<0.005$). When comparing patients with PD with healthy individuals, we found that genu and SW decreased in the PD group, while CCL and CL increased; however, these changes were not statistically significant except for GW. Mohammadi et al.[9] also found a positive relationship between CCL, CL, and CCW. Our findings support this result. We found a moderate positive correlation between CCL and CL in both the control group and the PD group.

Studies comparing patients with PD with healthy control groups have found that the corpus callosum thickness, particularly in the anterior half, is reduced in Parkinson's patients[10,11]. Significant decreases in volume in the anterior 2/5 of the corpus callosum and fractional anisotropy have also been observed in Parkinson's patients[2]. This is associated with impaired information processing in the prefrontal cortex, motor, and supplementary motor areas[12]. Gattellaro et al.[13], in their functional MRI study, suggested that the microstructure of the corpus callosum genu in patients with PD was impaired even at an early stage, while Guimarães et al.[3] suggested that changes in the corpus callosum, which they examined with diffusion tensor imaging, began to be observed at later stages. Furthermore, a clear connection between vascular parkinsonism and issues in the genu of the corpus callosum has been identified[14]. Reduced fiber density in the genu and body is related to gait asymmetry[2,15]. Our findings indicate that genu and RW are reduced in the PD group ($p<0.001$) and that the genu section is more affected in older patients with PD. The genu section of the corpus callosum is associated with cognitive functions, attention, and executive disorders; therefore, genu involvement may affect symptoms such as dementia, distractibility, and impaired control of planned movements[10,16].

Table 3. Comparing the angle values among different groups (°)

	Control group			PD group			
	Female Mean ± SD	Male Mean ± SD	Total Mean ± SD	Female Mean ± SD	Male Mean ± SD	Total Mean ± SD	p*
Angle 1	86.3±11.0	81.3±7.8	86.6±10.1	86.7±7.8	83.9±8.4	85.2±8.2	0.240
Angle 2	126.3±12.9	126.1±7.0	126.2±11.3	124.2±6.9	123.0±7.2	123.5±7.1	0.027
Angle 3	26.6±3.8	27.2±4.7	26.8±4.1	26.6±3.9	27.0±4.0	26.8±3.9	0.957
Angle 4	24.4±4.3	25.3±4.4	24.7±4.4	27.2±4.5	27.7±4.3	27.5±4.4	0.000
Angle 5	26.6±3.2	25.7±3.9	26.3±3.5	28.2±3.1	27.7±3.6	27.9±3.3	0.000

*: Independent sample t-test $p<0.05$, SD: Standard deviation, PD: Parkinson's disease

In the study by Bledsoe et al.[17], the corpus callosum in patients with PD was divided into five regions and examined using the diffusion tensor imaging method. The study showed an increase in axial diffusivity and a decrease in fractional anisotropy in the anterior 3/5 of the corpus callosum. These findings indicate damage to myelinated fibers and white matter atrophy. Our study results are also consistent with these findings. This supports the observation of a reduction in the number of fibers and microstructural atrophy in the affected regions identified through metric measurements.

In a study in which the distance from the vertex of the corpus callosum to the anterior commissure was evaluated as the CCH, it was reported that the CCH increased with age[18]. As in our study, in another study where the CCH was determined by measuring the distance between the tangent lines to the highest and lowest points of the corpus callosum, it was found that the height increased with age[19]. Our study revealed that height increased with age in both the control group and the group diagnosed with PD, with the group diagnosed with PD having a significantly greater mean CCH ($p<0.001$). This increase in height also resulted in a significant difference between the two groups in the average values of the FV and AIV parameters ($p<0.05$). Additionally, in patients with PD as CCH increased, RW and CL also increased, while GW decreased.

In some studies, the values measured as Angle 1 and Angle 2 have been expressed as the corpus callosum bending angle. In studies involving patients with schizophrenia spectrum disorders and niemann-pick type C, no significant differences were observed in Angle 1 with respect to age, sex, or between groups[20,21]. Similarly, in a study comparing patients with Williams syndrome to healthy individuals, no significant difference was found in terms of Angle 2[22]. In our study, while there was no difference in Angle 1 between sexes or groups ($p>0.05$), the value of Angle 2 was significantly lower in the PD group ($p=0.027$). Both angles were observed to be higher in the 41-50 age group of patients with PD and decreased with advancing age. This study found that the decrease in Angle 2 was more significant in the Parkinson's group compared to the control group, especially after the age of 41-50. This finding may indicate a potential increase in the bending of the corpus callosum due to the progression of PD.

Angle 5 indicates the position of the anterior part of the corpus callosum relative to the floor of the 4th ventricle[23]. In one study, frontal dysplasia was found to increase Angle 5, and no difference was observed between autistic and non-autistic individuals with macrocephaly[24]. In our study, the increase in the average value of Angle 5 in the PD group was found to be statistically significant ($p<0.001$), which may indicate an increased tendency for frontal localization of the corpus callosum in PD patients.

Study Limitations

This study has some limitations. First, the retrospective design limits the ability to control for potential confounding variables. Second, the evaluation was based solely on midsagittal MRI images, which may not fully reflect all microstructural changes in the corpus callosum. We believe that including clinical data such as disease duration, medication use, or cognitive status in future studies would allow for a more comprehensive analysis, and this study serves as a guiding basis for such research.

CONCLUSION

In conclusion, PD is a progressive neurodegenerative condition that affects daily activities and reduces quality of life, making early diagnosis crucial for successful treatment. Therefore, there is a necessity to conduct research on white matter, as developing new perspectives and focusing on new methods in this area is essential. The consistency of results across studies using different methodologies enhances the reliability of these findings. We believe our study is significant for supporting findings from other techniques, being one of the most comprehensive studies focusing specifically on the corpus callosum, and adding new measurement parameters to the literature.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Tekirdağ Namık Kemal University (decision no: 2021.74.03.14, date: 30.03.2021).

Informed Consent: The study is a retrospective study.

Footnotes

Authorship Contributions

Concept: D.T., A.Z., Design: D.T., A.Z., Data Collection or Processing: D.T., A.Z., S.A., Analysis or Interpretation: D.T., A.Z., S.A., Literature Search: D.T., A.Z., S.A., Writing: D.T., A.Z.

Conflict of Interest: No conflict of interest was declared by the authors.

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