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Retrospective evaluation of lateral ventricular volume in Parkinson's patients and control group on magnetic resonance images

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Abstract

Due to its flexible and expandable nature, the lateral ventricle volume has the potential to change in response to neurodegenerative diseases. Therefore, our study aims to calculate the lateral ventricle volume and its ratios to both the intracranial and cerebrum volumes and compare these measurements between Parkinson's patients and controls. By examining these ratios, we aim to better understand the relationship between lateral ventricle volume and brain structure in the context of Parkinson's disease. Magnetic resonance imaging of 54 Parkinson's patients (13 female; 41 male) and 26 healthy controls (8 female; 18 male) were included in the study. Lateral ventricle and intracranial volumes were calculated using the Cavalieri method in the ImageJ program on magnetic resonance images. Cerebrum volume was calculated using the BrainSuite program. It was observed that female patients with Parkinson's had a higher right-sided lateral ventricle volume than female controls. The right-sided lateral ventricle volume ratio to cerebrum volume and intracranial volume was also higher ($p<0.05$). Changes in ventricle volume are of great importance in diseases due to their relationship with anatomical structures. As seen in the results of our study, we think that the gender factor should be taken into account when evaluating the ventricle volume in neurodegenerative diseases.

Keywords: BrainSuite, ImageJ, Horos, cerebrum volume, intracranial volume

1. Introduction

Parkinson's disease is a neurodegenerative disorder that arises from the degeneration of dopaminergic neurons in the substantia nigra pars compacta region. The disease can cause various changes in the cortical and subcortical areas of the brain (1-3).

The lateral ventricle is a flexible and expandable structure located between the cortical and subcortical structures in the brain, which contains cerebrospinal fluid. The volume of this ventricle can vary depending on age, brain size, and morphology. An increase in lateral ventricle volume may be an important sign during the progression of neurodegenerative diseases such as Parkinson's disease (4-6).

Therefore, it is important to calculate the lateral ventricle volume and the ratio of the lateral ventricle volume to cerebral and intracranial volume in Parkinson's patients and compare it to healthy controls (4, 7-9). This study was designed to understand better the relationship between morphological changes in the brain and lateral ventricle volume in Parkinson's disease.

In this study, the lateral ventricle volume and the ratio of ventricle volume to cerebral and intracranial volume in Parkinson's patients were compared with those of healthy controls. Thus, the aim is to determine the relationship between structural changes in the brain due to Parkinson's disease and lateral ventricle volume. Understanding the effects of neurodegenerative diseases such as Parkinson's disease on brain morphology is important for diagnosis, monitoring, and treatment. This study shows that the increase in lateral ventricle volume in Parkinson's patients may be an important marker in the progression of the disease.

2. Materials and Methods

2.1. Participants and Data Collection

This study was approved by the Clinical Research Ethics Committee of Tokat Gaziosmanpaşa University (Approval Date: 02.03.2023, Project No: 23-KAEK-047). We enrolled 54 patients with Parkinson's disease who were diagnosed based on neurological examination and underwent routine brain MRI (magnetic resonance images) for diagnostic purposes at the Gaziosmanpasa University Faculty of Medicine between January 1st, 2013, and January 1st, 2023. The control group included 26 patients who underwent brain MRI for diagnostic purposes for various reasons but had no history of trauma or pathology. All images were retrospectively reviewed through the medical faculty patient tracking system, and six MRI images from the patient group and four MRI images from the control group were excluded from the study due to imaging artifacts. The study participants were aged between 42 and 80 years.

2.2. Automatic Segmentation Software: BrainSuite

To calculate the volume of the cerebrum, we used the

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BrainSuite software (version 19a), an automatic segmentation tool. The MR images were saved in Digital Imaging and Communication in Medicine (DICOM) format using the Horos program (version 4.3.1.). The images were then imported into ImageJ and saved in Analyze 7.5 format to be used in BrainSuite software. After completing the analysis, the cerebrum volume was obtained from the "roiwise.stats" file, which contains brain structure volumes and cortical thicknesses.

2.3. Manual Measurements with ImageJ

We manually measured the total intracranial volume and lateral ventricle using the ImageJ program (version 1.52a). To analyze the lateral ventricle, stack using the "Convert Images to Stack" function in the "Stacks" submenu. The threshold value was set to ensure that the images were converted to binary display that matched the original image (Fig. 1).

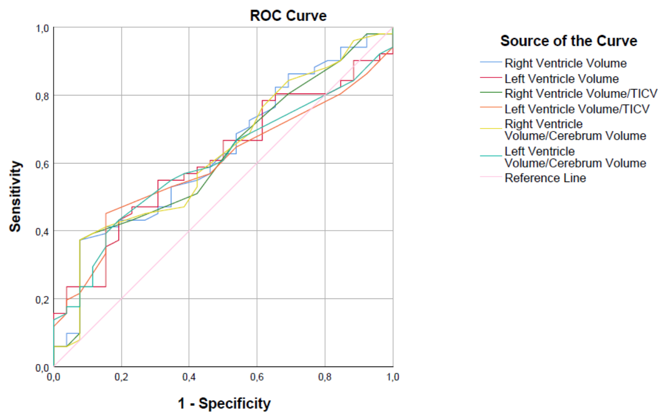

Fig. 1. Determination of lateral ventricle limits

We identified the lateral ventricle as the region of interest (ROI) for this study and outlined it manually on each lateral ventricle's boundaries using the "Polygon selection tool" in the "Analyze > Tools" menu. Each slice of the ROI was added to the ROI manager using the "Add" function. The area of each ROI was computed using the "Measure" function in the ROI manager menu.

The lateral ventricle was estimated by multiplying the section thickness with the total sectional surface area. The volume was calculated using the Cavalieri principle, based on the surface area multiplied by the cortical thickness. To compute the total volume of the lateral ventricle, we multiplied the sum of the areas (mm^2) of all the ROIs by the slice thickness (mm). This gave the total volume of the lateral ventricle (mm^3).

One of the first steps in the BrainSuite program was to define the skull borders, which were output as the "mask.nii.gz" file. This file, which contains the skull borders for each participant, was transferred to the ImageJ software. ImageJ measures the area inside the cranium using the Cavalieri principle. The area measurements of the intracranial cavity were calculated using the image series and the "adjust" and "threshold" tools in the "Image" menu, similar to the ventricle calculations.

2.4. Statistical Analysis

Statistical analysis was conducted using version 25.0 of SPSS (SPSS Inc., Chicago, IL). Data were analyzed per patient and on a normal and abnormal side basis. Categorical variables were described using frequency and percentage and numerical variables by the mean and standard deviation or median and minimum-maximum values. The independent sample median values were compared with the Mann-Whitney U Test. The study was performed at a 95% confidence level ($p < 0.05$ was considered statistically significant).

Receiver operating characteristic (ROC) analysis was also performed to evaluate the diagnostic performance of the variables. The area under the curve (AUC) was calculated for each variable, and the optimal cutoff point was determined based on the highest Youden index.

3. Results

Table 1 compares the measurements of right and left-sided lateral ventricle volumes, and lateral ventricle volume normalized to brain volume between the patients and control groups.

Table 1. Comparison of lateral ventricle volumes and volume ratios between patients and controls

	Patients (n=51)	Controls (n=26)	Test Ist.	p[1]
R Lateral Ventricle Volume (cm^3)	10.4 (1.9 - 37.3)/42.35	9.15 (3.1 - 24.7)/32.42	492.00	0.07
R Lateral Ventricle Volume/TICV	0.007 (0.001 - 0.024)/32.98	0.006 (0.002 -0.016)/42.07	506.50	0.09
R Lateral Ventricle Volume/Cerebrum Volume	0.013 (0.002 - 0.05)/42.26	0.011 (0.004 -0.033)/32.60	496.50	0.07
L Lateral Ventricle Volume (cm^3)	11.3 (1.9 - 36.5)/41.85	9 (4.3 - 23.4)/33.40	517.50	0.12
L Lateral Ventricle Volume /TICV	0.008 (0.001 - 0.024)/41.48	0.006 (0.003 -0.016)/34.13	536.50	0.17
L Lateral Ventricle Volume /Cerebrum Volume	0.015 (0.002 - 0.047)/41.71	0.012 (0.005 -0.031)/33.71	525.50	0.14

[1]Mann Whitney U testi, mean (min-mak)/mean rank, TICV: Total intracranial volume, R:Right-sided, L: Left-sided

Statistical analysis revealed that there were no significant differences between the two groups. However, compared to the controls, the patients had higher volumes of both right and left-sided lateral ventricles, as well as higher ratios of lateral ventricle volume to total intracranial volume (TICV) and cerebrum volume (Table 1).

Among female participants, the patients had significantly higher volumes of the right-sided lateral ventricle, as well as higher ratios of lateral ventricle volume to both total intracranial volume and cerebrum volume compared to the female controls ($p<0.05$) (Table 2).

Table 2. Comparison of patients and controls by gender for right-sided lateral ventricle volume normalized to brain volume and total intracranial volume

		Patients	Controls	Test Ist.	p[1]
R Lateral Ventricle Volume (cm^3)	Male	9.85(1.9 - 37.3)/29.50	9.5 (3.3 - 24.7)/26.39	304	0.505
	Female	13.8(4.4 - 18)/12.62	7.2 (3.1 - 10.5)/13.62	18	**0.013**
R Lateral Ventricle Volume /TICV	Male	0.006(0.001 - 0.024)/29.62	0.006 (0.002 - 0.016)/26.14	299.5	0.453
	Female	0.01 (0.003 - 0.015)/13.38	0.006 (0.002 - 0.008)/7.12	21	**0.025**
R Lateral Ventricle Volume /Cerebrum Volume	Male	0.012 (0.002 - 0.05)/29.79	0.011 (0.004 - 0.033)/25.78	293	0.389
	Female	0.02 (0.006 - 0.029)/13.35	0.011 (0.005 - 0.016)/7.19	21.5	**0.025**

[1]Mann Whitney U testi, mean (min-mak)/mean rank, TICV: Total intracranial volume, R:Right-sided, L: Left-sided

Regarding left-sided lateral ventricle volume and its ratios, no significant differences were found between female patients and female controls, as well as between male patients and male controls ($p>0.05$) (Table 3).

Table 3. Comparison of patients and controls by gender for left-sided lateral ventricle volume normalized to brain volume and total intracranial volume

		Patients	Controls	Test Ist.	p[1]
L Lateral Ventricle Volume (cm^3)	Male	11.3 (1.9 - 36.5)/29.38	10.5 (4.8 - 23.4)/26.64	308.5	0.557
	Female	12.5 (2.8 - 25.6)/13.08	6.75 (4.3 - 16.5)/7.62	25.0	0.053
L Lateral Ventricle Volume /TICV	Male	0.008 (0.001 - 0.024)/29.37	0.007 (0.003 - 0.016)/26.67	309.0	0.560
	Female	0.009 (0.002 - 0.02)/12.58	0.005 (0.003 - 0.012)/8.44	31.5	0.140
L Lateral Ventricle Volume /Cerebrum Volume	Male	0.015 (0.002 - 0.047)/29.61	0.013 (0.005 - 0.031)/26.17	300.0	0.461
	Female	0.019 (0.004 - 0.04)/15.58	0.01 (0.006 - 0.023)/8.44	31.5	0.140

[1]Mann Whitney U testi, mean (min-mak)/mean rank, TICV: Total intracranial volume, R:Right-sided, L: Left-sided

To evaluate the diagnostic accuracy of different measurements in distinguishing between patients and controls, we performed a receiver operating characteristic (ROC) analysis. This analysis included the measurements of both right and left-sided lateral ventricle volumes, lateral ventricle volume/total intracranial volume (TICV), and lateral ventricle volume/cerebrum volume ratios. The results are presented in a graph, where the true positive rate (sensitivity) is plotted on the y-axis, and the false positive rate (1-specificity) is plotted on the x-axis. The graph shows that the ROC curves for all the measurements are mainly concentrated in the upper left part of the graph, indicating good diagnostic accuracy. In other words, all the measurements have high sensitivity and specificity for distinguishing between patients and controls (Fig. 2).

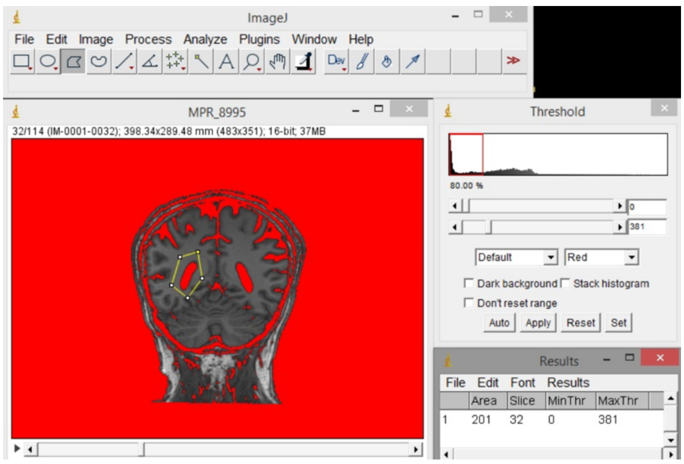

Fig. 2. ROC analysis graph

The diagnostic accuracy of different test result variables, including the right and left-sided lateral ventricle volumes, lateral ventricle volume/total intracranial volume (TICV), and lateral ventricle volume/cerebrum volume ratios, were assessed using the area under the curve (AUC) values. The table presents the AUC values, along with their standard errors, asymptotic significance, and 95% confidence intervals. The AUC values range from 0.595 to 0.629, indicating fair to moderate diagnostic accuracy for all the measurements. In other words, these measurements can be used to distinguish between patients and controls, but the accuracy may not be high enough for clinical use (Table 4).

Table 4. Analysis test results

Area Under the Curve					
				Asymptotic 95% Confidence Interval	
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Lower Bound	Upper Bound
R Lateral Ventricle Volume	0.629	0.066	0.065	0.5	0.758
R Lateral Ventricle Volume/TICV	0.61	0.065	0.117	0.483	0.737
R Lateral Ventricle Volume/Cerebrum Volume	0.618	0.066	0.092	0.489	0.747
L Lateral Ventricle Volume	0.595	0.064	0.173	0.469	0.721
L Lateral Ventricle Volume/TICV	0.626	0.066	0.073	0.496	0.755
L Lateral Ventricle Volume/Cerebrum Volume	0.604	0.064	0.139	0.478	0.73

The test result variable(s): R/L; lateral ventricle volume, lateral ventricle volume/TICV, lateral ventricle volume/cerebrum volume has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. a. Under the nonparametric assumption b. Null hypothesis: true area = 0.5

4. Discussion

The field of literature has extensively explored alterations in brain morphology associated with various diseases (10-13). These alterations may involve different structures, such as gray matter, white matter, and ventricle volume. In fact, changes in lateral ventricle volume can be due to changes in gray and white matter volume or can lead to alterations in these volumes (4, 9, 14-18). Furthermore, recent studies have discovered that changes in brain morphology are also linked to neurodegenerative (19-22) and psychiatric conditions (23-27). For example, Parkinson's disease is one of the neurodegenerative diseases that has been studied extensively in this context.

Our study compared the left and right-sided lateral ventricle volumes in patients with Parkinson's disease to those of a control group. We observed larger lateral ventricle volume in patients, but this difference was not statistically significant. However, we found that female patients had significantly higher right-side lateral ventricle volume, lateral ventricle volume/cerebrum volume, and lateral ventricle volume /TICV compared to the female controls. According to the ROC analysis, the range of AUC values was between 0.595 and 0.629, indicating an increase in this parameter, but it was not statistically significant.

Our study has yielded similar and different results compared to the literature. The study by Hikmet Kocaman et al. (2019) also compared lateral ventricle volume between Parkinson's patients and controls and reported no difference between the groups in total lateral ventricle volume. This finding is consistent with our study. However, when they analyzed the lateral ventricle by dividing it into sections, they observed that certain regions of the ventricle showed higher volume in Parkinson's patients. Although we did not segment the lateral ventricle in our study, we acknowledge this as a limitation, and future studies could benefit from a more specific segmentation analysis. The study highlights the importance of analyzing different regions of the brain, including the lateral ventricle, to understand the exact mechanism of Parkinson's disease. Hikmet Kocaman et al. found that although changes in certain regions of lateral ventricle volume may not cause a change in total lateral ventricle volume, they may be more significant. Therefore, a more comprehensive analysis of the brain may be necessary to fully understand the impact of Parkinson's disease on the brain (8). Other studies (15, 16, 28-31) have reported larger lateral ventricle volumes in Parkinson's patients compared to healthy controls. In a study by Liana et al., which is similar to ours, the lateral ventricle volume was compared between healthy controls and Parkinson's patients, and different results were obtained. The study was conducted on 35 patients (30). In the study by Richard et al., which was conducted on 50 patients, the Parkinson's group was further divided into subcategories (16). The difference in their findings compared to ours could be due to the smaller sample size used in their study. We believe that the results obtained from our study are more representative due to the larger sample size used in the analysis. Turi et al. reported a different result from our study, stating that the lateral ventricle volume of Parkinson's patients was higher than healthy controls. However, they used a different method from ours, using FreeSurfer to calculate lateral ventricle volume. Our study determined the lateral ventricle areas by examining them in sections and calculated the volume accordingly. In this study, the lateral ventricle volume was calculated automatically, which could be a potential source of difference between the results. Therefore, the difference in findings between our study and Turi et al.'s study may be attributed to differences in methodology (29).

However, we believe these findings are insufficient, as brain and cranium sizes can vary between individuals, particularly regarding age and sex (6, 14, 17, 21, 32, 33). Therefore, we have sought to normalize ventricle volume by considering its ratio to brain and cranium volumes. Our aim here is to eliminate differences that may arise between individuals and obtain more objective results.

In a study by Tolga and colleagues, they compared ventricle volumes between patients with Alzheimer's disease and controls. The results showed higher volumes in the patient group, but no significant differences in total intracranial volume between the two groups were found (34). It should be noted that normalizing ventricle volume by considering its ratio to intracranial volume is necessary, even if there are no differences in intracranial volume between patient and control groups. Normalization is a method used to eliminate differences between individuals. Therefore, comparing groups individually without considering volume ratios is generally not appropriate.

A recent study suggested that there is more volume increase in the contralateral ventricles in Parkinson's patients on the symptomatic side (16). Although we did not differentiate between symptomatic and asymptomatic sides, our findings showed that the right ventricle volume was significantly larger than the left.

In conclusion, our study provides evidence that changes in ventricle volume may be linked to Parkinson's disease, particularly in female patients. However, our study's lack of statistically significant results could be due to the small sample size. Therefore, future studies with larger sample sizes and more advanced imaging techniques are needed to confirm our findings and further explore the role of ventricle volume changes in Parkinson's disease.

It is important to note that our study had some limitations. Firstly, the small sample size limited the generalizability of our findings. Secondly, we only examined ventricle volume without considering other brain structures or functions. A more comprehensive brain morphology and function analysis would provide a more detailed understanding of the disease mechanism. Thirdly, we only included patients with idiopathic Parkinson's disease and did not examine other types of Parkinsonism. Lastly, our study did not differentiate between symptomatic and asymptomatic sides, which may have affected our findings.

Despite these limitations, our study contributes to the existing literature by highlighting the importance of considering gender and normalizing ventricle volume in studies of Parkinson's disease.

Considering all of this, it seems that lateral ventricle volume can be affected by factors such as neurodegenerative diseases, mental illnesses, aging, and sex. Therefore, lateral ventricle volume can be used as an important biomarker in investigating brain health and diseases.

The changes in ventricle volume are a crucial factor in many neurodegenerative diseases, as they are closely related to the underlying anatomical structures. Our study aimed to investigate the effect of ventricle volume on Parkinson's disease, which is one of the neurodegenerative diseases. Specifically, our analysis revealed that in Parkinson's disease female patients, the right-sided lateral ventricle volume and the ratios of lateral ventricle volume to both total intracranial volume and cerebrum volume were significantly higher compared to female controls. However, the difference in lateral ventricle volume between male patients and male controls was not statistically significant.

The implications of these findings are important, as they suggest that gender should be considered as a critical factor when assessing lateral ventricle volume in neurodegenerative diseases. This information can be useful in developing more personalized treatment plans for patients with these conditions.

Conflict of interest
The authors declared no conflict of interest.

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None to declare.

Authors' contributions
Concept: M.N., B.D., Design: M.N., B.D., Data Collection or Processing: M.N., B.D., Analysis or Interpretation: M.N., B.D., Literature Search: M.N., B.D., Writing: M.N., B.D.,

Ethical Statement
The study was carried out in conformity with the Declaration of Helsinki after obtaining the approval of Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (Date: 02.03.2023, Project No: 23-KAEK-047).

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