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# Comparison of detailed brain volume measurements in schizophrenia with healthy individuals

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## ABSTRACT

**Aims:** This study aims to provide insights into the preliminary and definitive diagnosis, treatment modalities, and elucidation of the underlying pathophysiological mechanisms of schizophrenia, alongside ongoing research efforts.

**Methods:** This retrospective study examined a cohort of 31 patients (17 male, 14 female) diagnosed with schizophrenia according to the criteria specified in the Diagnostic and Statistical Manual of Mental Disorders (DSM V) at the psychiatry clinic of the university hospital. The healthy control group, comprising 31 individuals (17 male, 14 female), was selected from archived records at the same hospital, with sociodemographic characteristics matching those of the patient group. High-resolution T1-weighted MRI images of the individuals were analyzed using the VolBrain AssemblyNet program.

**Results:** It has been observed that the volumes of various brain structures, including white matter (WM), gray matter (GM), subcortical GM, cortical GM, WM+GM, IC, total cerebrum, right cerebrum, left cerebrum, cerebrum WM, cerebrum GM, are significantly reduced ($p<0.05$) in patients diagnosed with schizophrenia compared to healthy controls. Additionally, volumes of cerebellar WM, GM, vermis, brainstem, accumbens, hippocampus, thalamus, ventral diencephalon, amygdala, and basal forebrain were found to be decreased in schizophrenia patients compared to healthy controls. Conversely, volumes of the pallidum, caudate, putamen, inferior lateral ventricle, lateral ventricle, third ventricle, fourth ventricle, and CSF were observed to be increased.

**Conclusion:** These findings underscore the widespread nature of neuroanatomical alterations in schizophrenia and highlight the importance of understanding these changes for elucidating the disorder's pathophysiology and developing targeted therapeutic interventions. Further research is warranted to explore the interplay of genetic, developmental, and environmental factors in schizophrenia.

**Keywords:** Schizophrenia, brain volume, VolBrain, volumetric measurements

## INTRODUCTION

Schizophrenia, characterized as a severe psychiatric disorder, impacts around 0.4% of the global populace.[1] Its onset often commences during early adulthood but can manifest in adolescence. Notably, its prevalence spans across all strata of society, irrespective of socioeconomic status. This disorder follows a chronic and recurrent trajectory, persisting throughout an individual's lifespan. Schizophrenia stands as a paramount mental health concern in contemporary society due to its profound ramifications.[2] These include diminished productivity, shortened life expectancy, substantial utilization of hospital resources, exorbitant healthcare expenditures, and elevated suicide rates. The multifaceted impact of schizophrenia underscores the imperative for comprehensive strategies encompassing research, clinical interventions, and public health initiatives to address its complexities effectively.[1,2]

Consequential behavioral findings have significantly propelled the investigation into the neurobiology of schizophrenia. Advanced brain imaging techniques allow the scrutinizing of brain structures within naturalistic settings through noninvasive means, a rapidly evolving field owing to technological advancements. The utility of brain imaging in elucidating schizophrenia and fostering novel therapeutic approaches lies in its capacity to reveal global aberrations throughout the brain while integrating regional, morphological, and physiological anomalies with findings

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from clinical and neurobehavioral studies.[3] This multifaceted approach facilitates a comprehensive understanding of the disorder, thereby offering avenues for innovative interventions and treatment strategies.

Due to its advantages, magnetic resonance imaging (MRI) has supplanted numerous conventional imaging modalities in contemporary medical practice across various diseases.[4] Foremost among these is its noninvasive nature, obviating the need for invasive procedures, and its inherent safety by being free from ionizing radiation exposure. Moreover, MRI offers superior soft tissue resolution, enabling precise visualization of anatomical structures.[5] Beyond morphological insights, MRI also furnishes functional information, thus affording a comprehensive understanding of tissue physiology. This amalgamation of benefits positions MRI as a pivotal diagnostic tool, facilitating anatomical delineation and functional assessment in clinical contexts.[6]

Extensive scholarly attention has been devoted to investigating central nervous system (CNS) manifestations in schizophrenia. However, uncertainties persist regarding discrepancies in brain volume measurements within the CNS. Leveraging MRI's enhanced soft tissue imaging capabilities, we aimed to scrutinize brain volumes with greater precision. Specifically, employing the volbrain method, we calculated the volumes of 238 different brain structures, focusing on white and gray matter volumes, in individuals diagnosed with schizophrenia. This study aims to provide insights into the preliminary and definitive diagnosis treatment modalities, elucidating the underlying pathophysiological mechanisms of schizophrenia and ongoing research efforts.

## METHODS

### Ethics

The study was carried out with the permission of the Atatürk University Faculty of Medicine Clinical Researches Ethics Committee (Date: 206.01.2023, Decision No: 18). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Participants

This retrospective study analyzed a cohort comprising 31 patients diagnosed with schizophrenia based on the diagnostic criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM V). These patients were under the care and follow-up of the Psychiatry Clinic at the University Hospital. The control group consisted of 31 participants retrieved from archival records at the University Hospital, matched with the patient group regarding sociodemographic characteristics. These controls were deemed healthy, with no reported health issues. The cohort distribution consists of 17 male and 14 female due to the higher number of male individuals with schizophrenia in the experimental group. The control group consisted of 17 male and 14 female individuals, consistent with the experimental group.

### MRI Protocol

MRI imaging protocol utilized in this study comprised high-resolution T1-weighted 3D magnetization prepared rapid gradient echo (MPRAGE) sequences for anatomical visualization. T1-weighted 3D MPRAGE sequences comprised retrospective data acquired during the routine acquisition process. The imaging parameters were as follows: sagittal orientation, repetition time (TR) of 1900 ms/2.84s, flip angle of 15 degrees, echo time (TE) of 2.67 ms, field of view (FOV) of 256 $mm^2$, matrix size of 256x256, acquisition of 160 slices, each with a thickness of 1 mm, and a spatial resolution of 1x1x1 $mm^3$ isotropic.[4]

### VolBrain Method

The study employed VolBrain (https://volbrain.net/), an open-access platform designed for automated segmentation of diverse brain structures. Utilizing default VolBrain T1-weighted volumetric images, total cerebrum volumetric analysis was conducted across the study groups. Additionally, the study utilized the mricloud method, a web-based software developed by Johns Hopkins University, for volume calculation incorporating brain parcellation in MR images. To facilitate volume calculation using VolBrain, MR images underwent conversion to either 'gz' or 'rar' format. The process involved a series of prescribed steps to enable accurate volumetric analyses. The process commences with the opening of a file denoted by the extension 'DICOMDIR' via a DICOM viewer software application. Subsequently, to visualize the anatomical structure, high-resolution T1-weighted 3D magnetization prepared rapid gradient echo (MPRAGE) images are accessed using the software 'mricron', culminating in the creation of a compressed file with a 'gz' extension in the FSL format. Following this initial step, the images, now converted to 'gz' format, are uploaded onto the VolBrain web interface. Registration procedures are executed, whereby the 'gz' extension files are submitted to the system for processing. Upon completion of the upload, the system initiates volumetric analyses for all brain regions, typically within a time frame ranging from 5 to 10 minutes. The resultant volumetric data are then compiled and saved in portable document format (PDF).

In this study, the AssemblyNet partition was selected from VolBrain measurements. AssemblyNet is a large CNN ensemble for 3D whole-brain MRI segmentation. Volumetric values of all parts of the brain were measured in cm3 and percentages, and total-right-left ratios were measured. A total of 462 different data were obtained from each participant. White matter (WM), grey matter (GM), subcortical GM, cortical GM, cerebellar GM, cerebro spinal fluid (CSF), brain (WM+GM), intracranial cavity (IC), cerebrum, cerebrum WM, cerebrum GM, cerebellum, cerebellum WM, cerebellum GM, vermis, brainstem were measured. Subcortical structures Accumbens, amygdala, basal forebrain, caudate, hippocampus, pallidum, putamen, thalamus, and ventral diencephalon (DC) were measured (Figure). Among the cortical structures, frontal lobe and frontal lobe parts, the frontal pole, gyrus rectus, opercular inferior frontal gyrus, orbital inferior frontal gyrus, triangular inferior frontal gyrus, medial frontal cortex, middle frontal gyrus, anterior orbital gyrus, lateral orbital gyrus, medial orbital gyrus, posterior orbital gyrus, precentral gyrus, precentral gyrus medial segment, subcallosal area, superior frontal gyrus, superior frontal gyrus medial segment, supplementary motor cortex were measured. Temporal lobe and fusiform gyrus, planum polare, planum temporale, inferior temporal gyrus, middle temporal gyrus, superior temporal gyrus, transverse temporal gyrus, and temporal pole were measured. The parietal lobe and angular gyrus, postcentral gyrus, postcentral gyrus medial segment, precuneus, superior parietal lobule, and supramarginal gyrus were measured. The occipital lobe and calcarine cortex, cuneus, lingual gyrus,

occipital fusiform gyrus, inferior occipital gyrus, middle occipital gyrus, superior occipital gyrus, and occipital pole were measured. The limbic cortex and entorhinal area, anterior cingulate gyrus, middle cingulate gyrus, posterior cingulate gyrus, and parahippocampal gyrus were measured. The insular and insular cortex parts, anterior insula, posterior insula, central operculum, frontal operculum, and parietal operculum were measured. CSF, inferior lateral ventricle, lateral ventricle, third ventricle, fourth ventricle, and external CSF were measured.[4]

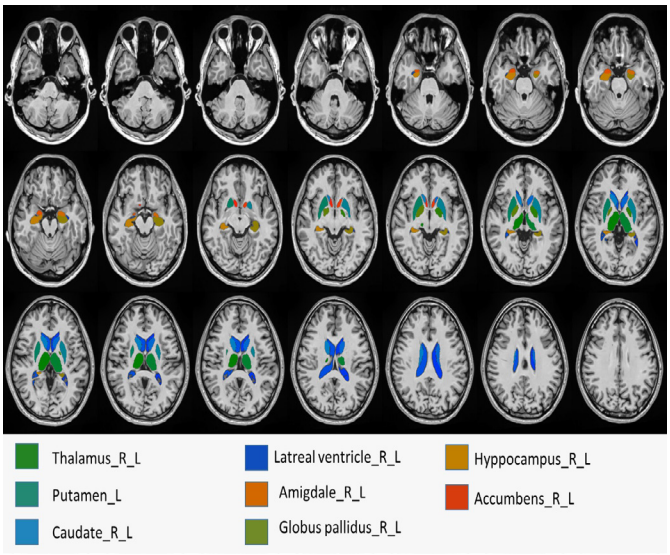


**Figure.** Volbrain images of subcortical structures measured in schizophrenia patients

### Statistical Analysis

All statistical analyses were conducted using IBM Corporation's Statistical Package for the Social Sciences (SPSS) version 22.0. Before data analysis, an a priori power analysis was performed using the G-Power 3.1.9.7 software to ensure adequate sample size. The analysis determined that with an effect size of 0.96, a power of 0.95 could be achieved at a 95% confidence interval, with a significance level set at 0.05. These parameters were selected to ensure robust statistical power and confidence in the findings.[7] Data were presented as means and standard deviations. Kurtosis and Skewness values revealed that our data showed normal distribution (between −2 and +2).[8] Since parametric test assumptions were met, the Student-t test determined The significant difference between independent groups. The significance level for all comparisons was set at $p < 0.05$.

## RESULTS

In this study, 17 male (54.84%) and 14 female (45.16%) patients diagnosed with schizophrenia were evaluated, alongside 17 male (54.84%) and 14 female (45.16%) healthy controls. The mean age of male schizophrenia patients in our study was calculated as 37.47±6.54 years, while for females, it was 38.43±7.89 years. For the control group, the mean age was 35.94±7.69 years for males and 34.14±7.26 years for females ($p>0.05$). The average body-mass index (BMI) among male schizophrenia patients was 29.53±2.43, and among female patients, it was 29.16±1.85. In the control group, the average BMI was 28.11±1.85 for males and 27.67±2.04 for females ($p>0.05$).

It has been observed that the volumes of various brain structures, including WM, GM, subcortical GM, cortical GM, WM+GM, IC, total cerebrum, right cerebrum, left cerebrum, cerebrum WM, cerebrum GM, are significantly reduced ($p<0.05$) in patients diagnosed with schizophrenia compared to healthy controls. CSF was observed to increase statistically significantly in both male and female patients with schizophrenia compared to the control group (Table 1). In both genders of schizophrenia patients, it was observed that volume measurements of the total, right, and left segments of the cerebellum, cerebellum WM, cerebellum GM, vermis, brainstem, accumbens, hippocampus, thalamus, and ventral DC regions, were lower compared to those in healthy individuals (Table 2, Figure). Specifically, statistically significant decreases in volume were determined for cerebellar WM, cerebellar GM, vermis, brainstem, accumbens, thalamus, and ventral DC in female schizophrenia patients ($p<0.05$). It has been observed that the volume measurements of the total, right, and left parts of the amygdala and basal forebrain, in schizophrenia patients are lower compared to healthy individuals. However, no statistically significant difference has been found (Table 2). It was determined that the volumes of the pallidum, caudate, putamen, inferior lateral ventricle, lateral ventricle, third ventricle, fourth ventricle, and external CSF in schizophrenia patients were higher than those in healthy individuals. This difference was found to be statistically significant, except for ventricular and pallidum volumes (Table 3). It has been noted that volume measurements of the frontal lobe, temporal lobe, occipital lobe, limbic cortex, and ınsular cortex are reduced in patients diagnosed with schizophrenia compared to healthy individuals. Specifically, in male patients with schizophrenia, significant reductions in volume measurements were observed in the triangular inferior frontal gyrus, anterior orbital gyrus, precentral gyrus medial segment, middle temporal gyrus, postcentral gyrus, precuneus, occipital lobe, occipital fusiform gyrus, and middle occipital gyrus ($p<0.05$). It was observed that the volume measurements of the frontal lobe, temporal lobe, occipital lobe, limbic cortex and insular cortex decreased statistically significantly in female patients with schizophrenia ($p<0.05$), (Table 4).

## DISCUSSION

There exists a substantial body of volumetric studies investigating morphological alterations in the brain, which hold significance in elucidating the etiopathogenesis of schizophrenia-an affliction characterized by both neurodevelopmental and neurodegenerative components.[3,5,7] However, to the best of our knowledge, there is a dearth of literature on studies employing the VolBrain AssemblyNet program, a novel automated measurement method, for comprehensive volume analysis across all brain regions. In studies conducted on individuals with schizophrenia, certain brain regions have been assessed, with specific affected areas identified; however, a comprehensive examination of all brain structures as a whole has been lacking. In this study, a total of 238 distinct brain areas were evaluated in both schizophrenia patients and healthy controls using the VolBrain method, marking one of the essential attempts to undertake such a comprehensive analysis. The objective of our investigation was to elucidate potential alterations in brain structure among individuals diagnosed with schizophrenia.

**Table 1. Comparison of overall brain volume measurements in schizophrenia and healthy individuals**

| | Schizophrenia male (X±SD) | Control male (X±SD) | p | Schizophrenia female (X±SD) | Control female (X±SD) | p |
|---|---|---|---|---|---|---|
| White matter $cm^3$ | 438.172±45.56 | 495.68±27.71 | 0.001** | 369.17±77.64 | 420.11±19.51 | 0.025* |
| White matter % | 31.61±3.08 | 34.21±2.39 | 0.010* | 31.51±3.85 | 32.59±2.73 | 0.398 |
| Grey matter $cm^3$ | 738.24±99.51 | 807.33±75.49 | 0.029* | 590.83±159.27 | 699.51±39.18 | 0.020* |
| Grey matter % | 53.12±5.64 | 55.53±3.36 | 0.140 | 49.53±6.71 | 54.17±3.27 | 0.028* |
| Subcortical $cm^3$ | 38.03±13.29 | 43.66±9.85 | 0.170 | 27.77±16.08 | 40.17±4.71 | 0.010* |
| Subcortical % | 2.76±0.92 | 3.03±0.69 | 0.373 | 2.24±1.24 | 3.12±0.48 | 0.019* |
| Cortical GM $cm^3$ | 589.35±81.14 | 649.41±65.71 | 0.024* | 470.07±125.34 | 554.91±36.92 | 0.022* |
| Cortical GM % | 42.37±4.38 | 44.67±3.18 | 0.090 | 39.46±5.31 | 42.95±2.65 | 0.037* |
| Cerebellar GM $cm^3$ | 110.84±14.62 | 114.25±17.81 | 0.546 | 92.98±22.94 | 104.42±9.93 | 0.099 |
| Cerebellar GM % | 7.97±0.78 | 7.83±0.74 | 0.585 | 7.83±0.72 | 8.09±0.81 | 0.380 |
| CSF $cm^3$ | 198.67±100.44 | 133.46±60.41 | 0.029* | 210.14±88.61 | 158.64±84.93 | 0.129 |
| CSF % | 14.06±6.29 | 9.02±3.49 | 0.007** | 17.83±6.06 | 11.91±5.43 | 0.011* |
| Brain (WM+GM) $cm^3$ | 1176.35±123.22 | 1303.01±84.13 | 0.001** | 959.94±218.74 | 1119.61±47.52 | 0.013* |
| Brain (WM+GM) % | 84.72±6.21 | 89.74±3.55 | 0.007** | 81.05±5.89 | 86.77±5.42 | 0.013* |
| Intracranial cavity $cm^3$ | 1391.75±147.62 | 1454.38±113.58 | 0.175 | 1182.96±253.49 | 1295.31±101.35 | 0.136 |
| Cerebrum total $cm^3$ | 1042.76±109.05 | 1165.55±74.38 | 0.001** | 848.98±191.95 | 991.77±47.18 | 0.012* |
| Cerebrum total % | 75.11±5.44 | 80.29±3.59 | 0.02* | 71.75±5.51 | 76.86±4.99 | 0.016* |
| Cerebrum right $cm^3$ | 544.42±49.16 | 576.99±37.32 | 0.037* | 447.25±118.77 | 512.32±48.92 | 0.069 |
| Cerebrum right % | 39.27±2.81 | 39.79±2.61 | 0.578 | 37.56±4.36 | 39.56±2.24 | 0.138 |
| Cerebrum left $cm^3$ | 498.34±94.34 | 588.55±43.44 | 0.001** | 401.72±106.49 | 479.44±59.95 | 0.025* |
| Cerebrum left % | 35.82±5.94 | 40.49±1.25 | 0.003** | 34.19±6.05 | 37.29±5.55 | 0.170 |
| Cerebrum total WM $cm^3$ | 390.53±101.13 | 472.48±30.62 | 0.003** | 320.97±105.36 | 396.68±20.09 | 0.014* |
| Cerebrum total WM % | 46.61±70.45 | 32.59±2.31 | 0.418 | 50.27±77.67 | 30.77±2.61 | 0.357 |
| Cerebrum right WM $cm^3$ | 206.03±59.89 | 236.01±17.92 | 0.057 | 176.36±67.36 | 202.07±13.82 | 0.174 |
| Cerebrum right WM % | 22.73±30.01 | 16.27±1.31 | 0.382* | 24.96±33.01 | 15.64±1.11 | 0.301 |
| Cerebrum left WM $cm^3$ | 184.51±53.22 | 236.47±14.21 | 0.001** | 144.61±61.96 | 194.61±17.64 | 0.007** |
| Cerebrum left WM % | 36.69±93.31 | 16.31±1.08 | 0.375 | 40.87±103.04629 | 15.13±1.91 | 0.358 |
| Cerebrum total GM $cm^3$ | 617.21±120.03 | 693.07±67.63 | 0.030* | 485.48±154.81 | 595.08±35.66 | 0.016* |
| Cerebrum total GM % | 44.32±7.76 | 47.71±3.52 | 0.112 | 40.71±8.63 | 46.08±2.87 | 0.036* |
| Cerebrum right GM $cm^3$ | 317.99±55.59 | 340.98±38.33 | 0.170 | 246.13±81.88 | 310.25±38.01 | 0.013* |
| Cerebrum right GM % | 22.96±3.81 | 23.51±2.51 | 0.620 | 20.40±4.53 | 23.92±1.67 | 0.011* |
| Cerebrum left GM $cm^3$ | 301.61±83.27 | 352.08±36.47 | 0.029* | 242.25±74.93 | 284.83±44.23 | 0.079 |
| Cerebrum left GM % | 21.55±5.19 | 24.18±1.31 | 0.052 | 20.53±4.52 | 22.16±3.81 | 0.315 |

X: Mean, SD: Standard deviation, CSF: Cerebro spinal fluid, WM: White matter, GM: Grey matter. **: p <0.01, *: p <0.05

Early investigations into brain volume measurements among individuals diagnosed with schizophrenia revealed heterogeneous findings, characterized by divergent alterations in specific brain regions. Some studies suggested an augmentation in WM volume in certain regions, juxtaposed with reductions in other areas.[9,10] However, a substantial body of contemporary research has provided converging evidence indicating a consistent diminution in WM volume among schizophrenia patients relative to healthy control counterparts. This prevailing trend towards reduced WM volume in schizophrenia has been substantiated by numerous recent studies, underscoring a growing consensus within the scientific community.[11-13] In this study, statistically significant reductions were observed in both the WM volumes in the right hemisphere, left hemisphere, and total WM in schizophrenia patients compared to those in the control group (Table 1). The observed reduction in WM volume represents a significant neuropathological hallmark of schizophrenia, implicating disrupted neural connectivity and communication across brain regions[12]. Understanding these neuroanatomical alterations is critical for elucidating the underlying pathophysiological mechanisms of schizophrenia and may hold implications for the development of novel therapeutic interventions aimed at ameliorating the associated cognitive and functional deficits in affected individuals.

In schizophrenia patients' studies, reductions in gray matter volume measurements, one of the most extensively studied metrics, have been consistently reported.[14,15] It has been suggested that this phenomenon may indicate structural alterations in the brain, particularly within regions associated with decision-making, emotion regulation, and cognitive control. In line with existing literature,[16] this study identified decreases in both right-left and total gray matter volume within cortical structures among individuals with schizophrenia compared to control groups.

**Table 2. Cerebellum. accumbens. hippocampus. Thalamus, ventral diencephalon volume, amygdala, and basal forebrain measurements comparison in schizophrenia and healthy individuals**

| | Schizophrenia Male (X±SD) | Control Male (X±SD) | p | Schizophrenia Female (X±SD) | Control Female (X±SD) | p |
|---|---|---|---|---|---|---|
| Cerebellum total $cm^3$ | 117.52±32.11 | 125.63±13.23 | 0.343 | 96.99±38.25 | 116.42±9.53 | 0.077 |
| Cerebellum total % | 10.24±5.49 | 8.63±0.61 | 0.241 | 10.33±6.11 | 9.03±0.91 | 0.435 |
| Cerebellum right $cm^3$ | 59.81±16.26 | 63.11±5.79 | 0.435 | 49.41±20.11 | 60.95±6.59 | 0.052 |
| Cerebellum right % | 4.99±1.88 | 4.34±0.31 | 0.169 | 4.97±2.11 | 4.71±0.39 | 0.653 |
| Cerebellum left $cm^3$ | 57.63±18.37 | 62.51±7.61 | 0.319 | 47.47±18.76 | 55.47±6.63 | 0.145 |
| Cerebellum left % | 4.77±1.77 | 4.29±0.32 | 0.284 | 4.79±1.89 | 4.32±0.67 | 0.390 |
| Cerebellum WM total $cm^3$ | 22.08±7.49 | 23.21±5.37 | 0.621 | 17.17±8.71 | 23.42±2.96 | 0.017* |
| Cerebellum WM total % | 1.59±0.54 | 1.61±0.39 | 0.909 | 1.39±0.65 | 1.82±0.28 | 0.035* |
| Cerebellum WM right $cm^3$ | 16.32±16.81 | 11.69±2.75 | 0.271 | 15.79±19.24 | 12.09±1.71 | 0.479 |
| Cerebellum WM right % | 1.21±1.36 | 0.81±0.21 | 0.243 | 1.27±1.52 | 0.93±0.14 | 04.25 |
| Cerebellum WM left $cm^3$ | 13.44±10.07 | 11.51±2.65 | 0.447 | 10.71±12.51 | 11.33±1.44 | 0.855 |
| Cerebellum WM left % | 0.99±0.81 | 0.79±0.19 | 0.338 | 0.87±0.99 | 0.88±0.15 | 0.972 |
| Cerebellum GM total $cm^3$ | 95.34±27.18 | 102.42±15.13 | 0.355 | 79.69±31.22 | 93.01±9.44 | 0.139 |
| Cerebellum GM total % | 7.01±1.11 | 7.02±0.62 | 0.985 | 6.96±1.18 | 7.21±0.77 | 0.525 |
| Cerebellum GM right $cm^3$ | 48.11±13.35 | 51.41±6.62 | 0.368 | 39.24±15.72 | 48.86±6.17 | 0.043* |
| Cerebellum GM right % | 4.22±2.32 | 3.52±0.26 | 0.228 | 4.24±2.59 | 3.77±0.34 | 0.508 |
| Cerebellum GM left $cm^3$ | 47.16±16.59 | 51.01±8.58 | 0.402 | 40.37±16.05 | 44.13±6.52 | 0.424 |
| Cerebellum GM left % | 3.38±0.93 | 3.49±0.36 | 0.669 | 3.45±0.88 | 3.43±0.59 | 0.962 |
| Vermis $cm^3$ | 10.68±3.08 | 11.83±2.83 | 0.269 | 7.44±4.13 | 11.41±1.26 | 0.002** |
| Vermis % | 0.77±0.23 | 0.81±0.13 | 0.596 | 0.64±0.31 | 0.88±0.07 | 0.010* |
| Brainstem $cm^3$ | 15.97±4.26 | 17.91±2.58 | 0.120 | 11.96±5.74 | 17.03±1.71 | 0.004** |
| Brainstem % | 1.15±0.32 | 1.23±0.12 | 0.359 | 1.03±0.44 | 1.31±0.11 | 0.031* |
| Accumbens total $cm^3$ | 0.78±0.36 | 0.93±0.28 | 0.206 | 0.48±0.36 | 0.77±0.23 | 0.018* |
| Accumbens total % | 0.05±0.02 | 0.06±0.02 | 0.338 | 0.03±0.02 | 0.06±0.02 | 0.031* |
| Accumbens right $cm^3$ | 0.38±0.16 | 0.43±0.15 | 0.327 | 0.22±0.16 | 0.38±0.11 | 0.006** |
| Accumbens right % | 0.02±0.01 | 0.03±0.01 | 0.509 | 0.01±0.01 | 0.02±0.01 | 0.015* |
| Accumbens left $cm^3$ | 0.41±0.21 | 0.49±0.14 | 0.147 | 0.25±0.21 | 0.39±0.14 | 0.050 |
| Accumbens left % | 0.02±0.01 | 0.03±0.01 | 0.244 | 0.02±0.01 | 0.03±0.01 | 0.063 |
| Hippocampus total $cm^3$ | 5.52±2.65 | 6.71±2.15 | 0.159 | 4.55±3.31 | 6.11±1.35 | 0.114 |
| Hippocampus total % | 0.39±0.18 | 0.46±0.14 | 0.246 | 0.37±0.26 | 0.47±0.11 | 0.178 |
| Hippocampus right $cm^3$ | 3.08±1.03 | 3.41±1.11 | 0.367 | 2.53±1.47 | 3.24±0.64 | 0.109 |
| Hippocampus right % | 0.22±0.07 | 0.23±0.07 | 0.599 | 0.21±0.11 | 0.25±0.05 | 0.177 |
| Hippocampus left $cm^3$ | 2.81±1.27 | 3.29±1.04 | 0.222 | 2.45±1.61 | 2.87±0.84 | 0.406 |
| Hippocampus left % | 0.21±0.08 | 0.22±0.06 | 0.354 | 0.21±0.12 | 0.22±0.07 | 0.532 |
| Thalamus total $cm^3$ | 14.15±3.92 | 16.02±3.06 | 0.132 | 10.43±5.21 | 14.96±1.31 | 0.004** |
| Thalamus total % | 5.59±18.72 | 1.11±0.22 | 0.332 | 6.36±20.68 | 1.15±0.11 | 0.355 |
| Thalamus right $cm^3$ | 7.26±1.95 | 7.87±1.72 | 0.340 | 5.66±2.63 | 7.35±0.98 | 0.033* |
| Thalamus right % | 3.51±12.24 | 0.54±0.12 | 0.327 | 4.05±13.51 | 0.57±0.07 | 0.343 |
| Thalamus left $cm^3$ | 6.89±2.14 | 8.14±1.39 | 0.051 | 4.76±3.24 | 7.61±0.47 | 0.003** |
| Thalamus left % | 0.79±1.15 | 0.56±0.11 | 0.422 | 0.73±1.31 | 0.58±.04 | 0.673 |
| Ventral DC total $cm^3$ | 8.78±2.61 | 9.32±1.83 | 0.492 | 6.47±3.11 | 9.19±1.13 | 0.005** |
| Ventral DC total % | 0.63±0.18 | 0.64±0.13 | 0.874 | 0.52±0.23 | 0.71±0.07 | 0.009** |
| Ventral DC right $cm^3$ | 4.38±1.33 | 4.54±1.06 | 0.710 | 3.48±1.47 | 4.51±0.59 | 0.022* |
| Ventral DC right % | 0.31±0.09 | 0.31±0.07 | 0.942 | 0.28±0.11 | 0.34±0.04 | 0.034* |
| Ventral DC left $cm^3$ | 4.29±1.53 | 4.78±0.79 | 0.256 | 2.86±2.09 | 4.67±0.56 | 0.004** |
| Ventral DC left % | 0.31±0.11 | 0.33±0.05 | 0.531 | 0.23±0.16 | 0.36±0.03 | 0.013* |
| Amygdala total $cm^3$ | 1.63±0.83 | 1.92±0.56 | 0.249 | 1.22±0.98 | 1.58±0.47 | 0.224 |
| Amygdala total % | 0.12±0.04 | 0.13±0.03 | 0.657 | 0.11±0.07 | 0.12±0.04 | 0.532 |
| Amygdala right $cm^3$ | 0.85±0.41 | 0.98±0.31 | 0.290 | 0.61±0.49 | 0.83±0.27 | 0.164 |
| Amygdala right % | 0.06±0.02 | 0.068±0.02 | 0.422 | 0.05±0.03 | 0.06±0.02 | 0.228 |
| Amygdala left $cm^3$ | 0.78±0.44 | 0.93±0.26 | 0.225 | 0.61±0.48 | 0.75±0.29 | 0.346 |
| Amygdala left % | 0.11±0.17 | 0.06±0.01 | 0.396 | 0.11±0.19 | 0.05±0.02 | 0.398 |
| Basal forebrain total $cm^3$ | 0.50±0.28 | 0.63±0.14 | 0.089 | 0.42±0.27 | 0.52±0.17 | 0.167 |
| Basal forebrain total % | 0.03±0.01 | 0.04±0.01 | 0.217 | 0.03±0.02 | 0.03±0.01 | 0.353 |
| Basal forebrain right $cm^3$ | 0.20±0.14 | 0.27±0.08 | 0.109 | 0.17±0.12 | 0.23±0.10 | 0.106 |
| Basal forebrain right % | 0.01±0.01 | 0.01±0.01 | 0.149 | 0.01±0.01 | 0.01±0.01 | 0.346 |
| Basal forebrain left $cm^3$ | 0.32±0.30 | 0.39±0.26 | 0.505 | 0.28±0.34 | 0.29±0.08 | 0.529 |
| Basal forebrain left % | 0.02±0.02 | 0.02±0.02 | 0.720 | 0.02±0.02 | 0.02±0.01 | 0.593 |

X: Mean, SD: Standard deviation, CSF: Cerebro spinal fluid, WM: White matter, GM: Grey matter. **: p <0.01, *: p <0.05

**Table 3. Comparison of volume measurements of caudate, pallidum, and putamen and ventricles in schizophrenia and healthy individuals**

| | Schizophrenia Male (X±SD) | Control Male (X±SD) | p | Schizophrenia Female (X±SD) | Control Female (X±SD) | p |
|---|---|---|---|---|---|---|
| Caudate total $cm^3$ | 6.30±1.21 | 5.04±2.13 | 0.042* | 5.48±1.02 | 3.23±2.54 | 0.005** |
| Caudate total % | 0.44±0.06 | 0.35±0.15 | 0.031* | 0.41±0.03 | 0.25±0.21 | 0.008** |
| Caudate right $cm^3$ | 3.17±0.55 | 2.52±1.02 | 0.028* | 2.73±0.55 | 1.62±1.36 | 0.009** |
| Caudate right % | 0.22±0.02 | 0.17±0.07 | 0.020* | 0.21±0.02 | 0.12±0.11 | 0.012* |
| Caudate left $cm^3$ | 3.13±0.66 | 2.52±1.22 | 0.080 | 2.74±0.48 | 1.61±1.33 | 0.006** |
| Caudate left % | 0.22±0.03 | 0.17±0.08 | 0.061 | 0.21±0.01 | 0.12±0.11 | 0.009** |
| Pallidum total $cm^3$ | 2.99±0.49 | 2.51±1.20 | 0.137 | 2.63±0.76 | 2.08±1.22 | 0.167 |
| Pallidum total % | 0.21±0.02 | 0.67±2.01 | 0.356 | 0.20±0.05 | 0.76±2.20 | 0.353 |
| Pallidum right $cm^3$ | 1.55±0.25 | 1,26±0.56 | 0.058 | 1.39±0.36 | 1.07±0.61 | 0.106 |
| Pallidum right % | 0.11±0.01 | 0.55±1.91 | 0.348 | 0.10±0.02 | 0.65±2.11 | 0.346 |
| Pallidum left $cm^3$ | 1.44±0.43 | 1.33±0.50 | 0.492 | 1.23±0.59 | 1.10±0.53 | 0.529 |
| Pallidum left % | 0.10±0.02 | 0.11±0.09 | 0.630 | 0.09±0.04 | 0.11±0.10 | 0.593 |
| Putamen total $cm^3$ | 8.73±1.53 | 7.99±2.88 | 0.357 | 8.01±1.71 | 6.05±2.93 | 0.042* |
| Putamen total % | 0.63±0.08 | 0.55±0.21 | 0.181 | 0.59±0.11 | 0.47±0.23 | 0.102 |
| Putamen right $cm^3$ | 4.53±0.62 | 4.11±1.33 | 0.249 | 4.22±0.84 | 3.36±1.61 | 0.091 |
| Putamen right % | 0.32±0.03 | 0.28±0.09 | 0.117 | 0.31±0.05 | 0.26±0.12 | 0.182 |
| Putamen left $cm^3$ | 4.21±1.06 | 3.88±1.74 | 0.524 | 3.77±1.34 | 2.68±1.96 | 0.099 |
| Putamen left % | 0.31±0.06 | 0.27±0.12 | 0.349 | 0.27±0.09 | 0.21±0.15 | 0.175 |
| Inf. lateral ventricle total $cm^3$ | 1.03±0.71 | 0.96±0.57 | 0.737 | 0.83±0.74 | 1.04±0.94 | 0.523 |
| Inf. lateral ventricle total % | 0.07±0.04 | 0.06±0.03 | 0.633 | 0.06±0.05 | 0.07±0.06 | 0.564 |
| Inf. lateral ventricle right $cm^3$ | 0.56±0.41 | 0.54±0.36 | 0.872 | 0.48±0.47 | 0.56±0.31 | 0.611 |
| Inf. lateral ventricle right % | 0.03±0.02 | 0.03±0.02 | 0.767 | 0.03±0.03 | 0.04±0.02 | 0.652 |
| Inf. lateral ventricle left $cm^3$ | 0.47±0.31 | 0.41±0.26 | 0.601 | 0.34±0.31 | 0.47±0.71 | 0.540 |
| Inf. lateral ventricle left % | 0.03±0.02 | 0.02±0.01 | 0.517 | 0.02±0.02 | 0.03±0.05 | 0.580 |
| Lateral ventricle total $cm^3$ | 20.21±11.61 | 16.16±14.45 | 0.375 | 23.09±15.47 | 20.21±21.01 | 0.681 |
| Lateral ventricle total % | 1.39±0.74 | 1.08±0.88 | 0.266 | 2.02±1.28 | 1.51±1.46 | 0.330 |
| Lateral ventricle right $cm^3$ | 9.63±6.13 | 7.95±8.26 | 0.507 | 12.17±10.17 | 9.27±10.12 | 0.457 |
| Lateral ventricle right % | 0.65±0.36 | 0.52±0.51 | 0.398 | 1.03±0.76 | 0.69±0.71 | 0.231 |
| Lateral ventricle left $cm^3$ | 10.57±8.77 | 8.21±6.28 | 0.371 | 10.92±6.12 | 10.92±11.13 | 0.952 |
| Lateral ventricle left % | 0.73±0.57 | 0.55±0.38 | 0.272 | 0.98±0.64 | 0.81±0.77 | 0.518 |
| Third ventricle total $cm^3$ | 1.08±0.87 | 0.89±0.65 | 0.472 | 0.93±0.91 | 1.09±0.99 | 0.668 |
| Third ventricle total % | 0.07±0.05 | 0.06±0.04 | 0.369 | 0.07±0.06 | 0.08±0.06 | 0.704 |
| Fourth ventricle total $cm^3$ | 1.51±0.77 | 1.36±0.45 | 0.517 | 1.21±0.92 | 1.62±0.98 | 0.260 |
| Fourth ventricle total $cm^3$ | 0.11±0.05 | 0.09±0.03 | 0.392 | 0.09±0.07 | 0.12±0.06 | 0.339 |
| External CSF total $cm^3$ | 170.74±93.81 | 114.07±50.17 | 0.035* | 173.27±83.39630 | 134.69±78.26 | 0.048* |
| External CSF total % | 11.87±5.71 | 7.72±2.89 | 0.038* | 14.68±5.76 | 10.11±5.07 | 0.035* |

X: Mean, SD: Standard deviation, CSF: Cerebro spinal fluid, **: p <0.01, *: p <0.05

CSF is vital for maintaining the structural integrity, metabolic balance, and physiological function of the brain and spinal cord. Any disruption in the dynamics or composition of CSF within the brain and spinal cord can significantly contribute to the development of various neurological disorders. Hence, CSF is one of the primary parameters measured in studies pertaining to schizophrenia in the existing literature. Some studies have reported that CSF volume remains unchanged in schizophrenia patients compared to healthy controls,[17] while a majority of recent studies indicate an increase in CSF volume.[18,19] In this study, a statistically significant increase in CSF volume was observed in both genders among schizophrenia patients.

The cerebellum, recognized as a densely organized structure, encompasses many functions spanning movement coordination, emotional processing, planning, and perception. Existing literature has consistently reported reductions in both white matter and gray matter volumes within the cerebellum in studies investigating individuals diagnosed with schizophrenia.[20,21] In the context of this study, analyses revealed decreases in cerebellar white matter, gray matter, and total volume among schizophrenia patients compared to a control group. Notably, the reduction in cerebellar volume observed in female schizophrenia patients reached statistical significance. The cerebellum's multifaceted role underscores its significance in understanding the neurobiology of schizophrenia. The identified volumetric reductions in white and gray matter within this structure suggest potential disruptions across a spectrum of cognitive and affective processes implicated in schizophrenia.

**Table 4. Comparison of volume measurements of frontal lobe, temporal lobe, occipital lobe, limbic cortex, and insular cortex in schizophrenia and healthy individuals**

| Cortical | Schizophrenia male (X±SD) | Control male (X±SD) | p | Schizophrenia female (X±SD) | Control female (X±SD) | p |
|---|---|---|---|---|---|---|
| Frontal lobe | 185.56±51.48 | 208.81±18.52 | 0.089 | 143.07±56.54 | 183.43±13.64 | 0.015* |
| Frontal pole | 7.31±2.36 | 8.01±1.48 | 0.304 | 5.46±1.78 | 7.07±1.21 | 0.009** |
| Gyrus rectus | 4.15±1.42 | 4.61±1.41 | 0.361 | 2.78±1.71 | 4.41±0.51 | 0.002** |
| Opercular inf. frontal gyrus | 6.22±2.27 | 7.28±1.23 | 0.100 | 5.36±2.68 | 6.43±1.01 | 0.173 |
| Orbital inf. frontal gyrus | 2.87±0.85 | 3.55±1.13 | 0.058 | 2.41±1.11 | 2.81±0.62 | 0.482 |
| Triangular inf. frontal gyrus | 6.96±2.15 | 8.45±1.52 | 0.026* | 6.28±2.06 | 6.81±1.77 | 0.481 |
| Medial frontal cortex | 3.51±1.34 | 3.89±1.41 | 0.430 | 2.27±1.67 | 3.61±0.96 | 0.016* |
| Middle frontal gyrus | 41.69±17.96 | 45.66±4.95 | 0.387 | 35.17±15.71 | 38.03±4.66 | 0.519 |
| Anterior orbital gyrus | 4.37±1.61 | 5.41±1.07 | 0.036* | 3.36±1.44 | 4.23±0.75 | 0.055 |
| Lateral orbital gyrus | 5.03±1.54 | 5.61±1.01 | 0.210 | 3.66±1.77 | 4.77±1.04 | 0.056 |
| Medial orbital gyrus | 8.66±2.83 | 9.67±1.65 | 0.211 | 6.22±3.28 | 9.21±1.01 | 0.003** |
| Posterior orbital gyrus | 7.31±2.65 | 7.12±1.11 | 0.799 | 5.38±3.53 | 6.58±1.11 | 0.237 |
| Precentral gyrus | 25.92±7.92 | 29.53±3.45 | 0.095 | 19.01±8.51 | 26.02±1.91 | 0.006** |
| Precentral gyrus medial seg. | 5.39±1.13 | 6.08±0.77 | 0.047* | 4.13±1.85 | 5.37±0.75 | 0.028* |
| Subcallosal area | 2.26±0.75 | 2.41±0.86 | 0.586 | 1.82±0.96 | 2.23±0.94 | 0.272 |
| Sup. frontal gyrus | 31.29±8.28 | 35.07±4.88 | 0.116 | 23.94±8.55 | 31.37±4.35 | 0.008** |
| Sup. frontal gyrus medial seg. | 13.04±4.11 | 14.81±2.58 | 0.145 | 9.59±4.18 | 13.49±2.27 | 0.005** |
| Supplementary motor cortex | 12.12±1.74 | 11.61±2.16 | 0.454 | 9.32±2.71 | 10.92±1.61 | 0.069 |
| Temporal lobe | 114.84±33.89 | 132.51±17.43 | 0.065 | 88.33±34.73 | 109.07±12.81 | 0.046* |
| Fusiform gyrus | 16.08±5.31 | 18.67±2.52 | 0.079 | 12.94±4.12 | 14.86±3.15 | 0.178 |
| Planum polare | 3.53±1.31 | 4.31±1.03 | 0.067 | 2.54±1.47 | 3.87±0.84 | 0.007** |
| Planum temporale | 8.57±19.84 | 4.31±1.89 | 0.384 | 8.58±22.15 | 3.21±0.51 | 0.373 |
| Inf. temporal gyrus | 26.13±9.64 | 29.17±3.97 | 0.238 | 21.35±7.77 | 24.23±3.79 | 0.225 |
| Middle temporal gyrus | 30.56±6.84 | 34.84±4.84 | 0.043* | 22.76±7.58 | 28.58±3.66 | 0.016* |
| Sup. temporal gyrus | 14.57±4.31 | 16.54±3.01 | 0.133 | 11.11±5.03 | 13.87±2.67 | 0.080 |
| Transverse temporal gyrus | 3.08±1.04 | 3.17±0.96 | 0.790 | 2.27±1.08 | 2.61±0.66 | 0.334 |
| Temporal pole | 18.42±5.05 | 21.47±3.69 | 0.054 | 14.21±5.81 | 17.82±1.18 | 0.031* |
| Parietal lobe | 118.73±22.15 | 133.74±21.98 | 0.056 | 95.31±29.61 | 112.91±10.25 | 0.045* |
| Angular gyrus | 25.69±11.97 | 29.33±10.86 | 0.360 | 21.81±12.32 | 22.36±3.71 | 0.874 |
| Postcentral gyrus | 22.11±6.62 | 25.76±3.11 | 0.048* | 16.41±7.45 | 21.96±2.52 | 0.014* |
| Postcentral gyrus medial seg. | 2.08±0.78 | 2.35±0.41 | 0.218 | 1.73±1.21 | 2.16±0.38 | 0.217 |
| Precuneus | 23.63±5.56 | 28.45±7.04 | 0.034* | 17.14±6.57 | 23.29±2.73 | 0.003** |
| Sup. parietal lobule | 24.23±7.85 | 27.41±4.71 | 0.162 | 20.71±8.29 | 24.75±4.24 | 0.116 |
| Supramarginal gyrus | 18.67±4.17 | 20.42±3.73 | 0.207 | 14.71±4.89 | 18.36±2.71 | 0.021* |
| Occipital lobe | 87.07±23.78 | 100.34±12.07 | 0.049* | 70.12±29.47 | 86.06±10.17 | 0.067 |
| Calcarine cortex | 8.33±2.25 | 9.05±1.69 | 0.300 | 6.56±2.65 | 7.05±1.42 | 0.551 |
| Cuneus | 10.11±3.11 | 10.83±2.91 | 0.485 | 7.04±4.24 | 10.52±2.17 | 0.011* |
| Lingual gyrus | 18.19±5.36 | 20.29±2.81 | 0.164 | 13.46±6.35 | 17.75±3.02 | 0.031* |
| Occipital fusiform gyrus | 8.96±2.63 | 11.43±2.51 | 0.009** | 8.06±3.58 | 8.67±1.07 | 0.548 |
| Inf. occipital gyrus | 16.42±6.53 | 17.84±5.11 | 0.487 | 15.41±9.03 | 15.32±2.49 | 0.975 |
| Middle occipital gyrus | 11.81±3.39 | 14.81±2.83 | 0.009** | 9.05±4.14 | 11.91±2.06 | 0.029* |
| Sup. occipital gyrus | 8.86±2.25 | 9.98±1.67 | 0.110 | 7.34±2.53 | 8.95±1.79 | 0.064 |
| Occipital pole | 5.24±1.58 | 6.11±1.41 | 0.104 | 4.21±2.32 | 5.86±1.48 | 0.034* |
| Limbic cortex | 38.04±11.74 | 43.86±6.99 | 0.089 | 30.96±13.05 | 37.26±3.66 | 0.094 |
| Entorhinal area | 3.79±1.31 | 3.77±0.63 | 0.966 | 2.96±1.63 | 3.81±0.71 | 0.085 |
| Anterior cingulate gyrus | 9.73±3.18 | 11.11±2.36 | 0.160 | 7.50±3.53 | 9.37±1.92 | 0.094 |
| Middle cingulate gyrus | 9.22±2.42 | 10.78±2.25 | 0.061 | 7.25±3.35 | 8.84±1.69 | 0.126 |
| Posterior cingulate gyrus | 9.17±2.95 | 10.91±3.59 | 0.133 | 8.21±3.16 | 8.52±0.79 | 0.717 |
| Parahippocampal gyrus | 6.29±2.02 | 7.27±1.31 | 0.103 | 5.24±2.03 | 6.71±0.75 | 0.018* |
| Insular cortex | 28.08±9.11 | 30.13±7.93 | 0.490 | 21.11±9.63 | 26.15±4.45 | 0.087 |
| Anterior insula | 7.76±2.65 | 8.33±1.82 | 0.475 | 5.93±2.98 | 7.55±1.59 | 0.085 |
| Posterior insula | 4.25±1.33 | 4.46±1.26 | 0.640 | 3.01±1.51 | 4.07±0.76 | 0.026* |
| Central operculum | 7.66±2.19 | 8.31±2.26 | 0.402 | 5.97±2.36 | 6.72±1.06 | 0.591 |
| Frontal operculum | 3.66±1.38 | 3.99±1.37 | 0.491 | 3.01±1.46 | 3.57±1.12 | 0.263 |
| Parietal operculum | 4.72±1.86 | 5.02±1.87 | 0.653 | 3.18±1.67 | 4.23±0.75 | 0.043* |

X: Mean, SD: Standard deviation, Sup: Superior, Inf: Inferior, Seg: Segment, **: p <0.01, *: p <0.05

Research investigating brainstem volume measurements in schizophrenia patients has consistently demonstrated a reduction compared to control groups, a phenomenon also observed in association with various other psychiatric conditions.[22] In alignment with existing literature, this study similarly identified decreased brainstem volumes among schizophrenia patients compared to the control group.

The nucleus accumbens, interconnected with various brain regions, particularly the limbic system, is pivotal in modulating the reward system, motivation, pleasure, addiction, and emotional functions. Existing literature indicates a consistent finding of reduced volume in the accumbens among schizophrenia patients compared to healthy controls.[23] This study observed a similar reduction in accumbens volume in schizophrenia patients relative to healthy controls. Additionally, statistically significant decreases in accumbens volume were noted among female schizophrenia patients.

The thalamus plays a pivotal role in processing and transmitting sensory information. Moreover, it influences cognitive processes encompassing memory, attention, language, and emotional functions. Given the presence of cognitive and emotional aberrations in individuals with schizophrenia, the association between the thalamus and schizophrenia has garnered attention. Numerous studies have demonstrated a reduction in thalamic volume among schizophrenia patients.[24,25] In this study, it is reported that thalamic volume is diminished in both male and female schizophrenia patients and statistically significant differences were found in women.

The term 'ventral DC' does not refer to a singular anatomical structure but rather encompasses a group of structures that are not readily distinguishable with standard MRI imaging. This composite region includes the hypothalamus, mammillary body, subthalamic nuclei, substantia nigra, red nucleus, lateral geniculate nucleus, and medial geniculate nucleus. Additionally, white matter areas such as the zona incerta, cerebral peduncle (crus cerebri), lenticular fasciculus, and medial lemniscus are encompassed within this area. The optic tract is also considered part of the ventral diencephalon in its most anterior extent. Each structure exhibits temporal variability within the ventral diencephalon, leading to considerable variation in its composition across different MRI slices. The ventral diencephalon houses structures integral to functions, including sensory relay, motor control, autonomic regulation, hormone secretion, and various aspects of cognition and emotion In the literature, studies investigating ventral diencephalon volume measurements in patients with schizophrenia report divergent findings, encompassing observations of both volume increases[26] and decreases,[27] as well as instances where no significant change is noted.[28] This study observed smaller ventral diencephalon volume measurements in schizophrenia patients compared to healthy controls. Several factors may contribute to the observed smaller volume of the ventral diencephalon in individuals with schizophrenia compared to healthy controls. However, the precise mechanisms underlying this difference remain incompletely understood and likely involve a multifaceted interplay of genetic predispositions, developmental abnormalities, environmental influences, and neurobiological alterations.

In addition to regulating motor movements, the basal ganglia significantly contribute to various cognitive processes such as decision-making and behavioral planning. These nuclei facilitate these pivotal functions through intricate communication among themselves and with the cortex. While the basal ganglia predominantly control motor functions via the dorsal corticostriatal circuit, they also play a crucial role in cognitive and sensory functions through the ventral corticostriatal circuit. Notably, while the caudate nucleus, one of the two components of the striatum, is particularly implicated in the ventral circuit, the putamen, the other component, predominantly governs motor functions within the dorsal circuit. Recent studies have underscored disruptions in these circuits across various psychiatric disorders, notably schizophrenia. Numerous investigations focusing on basal ganglia volume measurements in schizophrenia patients consistently report increases in both caudate and putamen volumes compared to healthy controls.[29,30] Consistent with the prevailing literature, this study reveals increases in pallidum, caudate, and putamen volumes among schizophrenia patients when compared to the control group. However, these increases are statistically significant in both sexes only in the caudate nucleus.

In the literature, alterations in the ventricular system have been extensively investigated in patients with schizophrenia since the inception of such studies.[31] Primarily, volume measurements of the lateral and third ventricles have been the focus of examination.[32] Previous studies have consistently reported enlarged ventricular volumes in schizophrenia patients compared to healthy individuals. This study assessed volumes of the inferior lateral ventricle, lateral ventricle, third ventricle, and fourth ventricle. It was observed that all ventricular volumes were greater in schizophrenia patients when compared to healthy controls, albeit without achieving statistical significance.

In the literature, schizophrenia is characterized by widespread alterations in brain morphology, with volumetric reductions noted across various brain regions in both male and female patients when compared to healthy controls.[3,17-19,28] In this study, in male patients with schizophrenia compared to healthy controls, volume reductions are noted across various brain regions, including the frontal lobe, temporal lobe, parietal lobe, occipital lobe, limbic cortex, and insular cortex. Furthermore, statistically significant decreases in the volumes of specific regions such as the triangular inferior frontal gyrus, anterior orbital gyrus, medial segment of the precentral gyrus, middle temporal gyrus, postcentral gyrus, precuneus, occipital fusiform gyrus, and middle occipital gyrus are observed when compared to healthy controls. In female patients with schizophrenia compared to healthy controls, there are notable volumetric reductions observed across a range of brain regions. These reductions encompass the frontal lobe, including the frontal pole, gyrus rectus, medial frontal cortex, medial orbital gyrus, precentral gyrus, and its medial segment, as well as the superior frontal gyrus and its medial segment. Similarly, reductions are evident in the temporal lobe, covering the planum polare, middle temporal gyrus, and temporal pole. Additionally, decreases in volume are observed in the parietal lobe, postcentral gyrus, precuneus, supramarginal gyrus, cuneus, lingual gyrus, middle occipital gyrus, occipital pole, parahippocampal gyrus, posterior insula, and parietal operculum. These findings underscore the widespread alterations in brain morphology associated with schizophrenia, highlighting the complex neuropathological underpinnings of the disorder.

## CONCLUSION

The findings of this study provide a comprehensive insight into the complex neuroanatomical alterations associated with schizophrenia. Utilizing the novel automated measurement method of the VolBrain AssemblyNet program, this research encompassed a thorough examination of 238 distinct brain areas, revealing significant volumetric changes across various structures. Consistent with existing literature, reductions in cerebellar WM, cerebellar GM, vermis, brainstem, accumbens, hippocampus, thalamus, and ventral DC, as well as changes in the amygdala and basal forebrain, were detected in schizophrenia. Increases in pallidum, caudate, putamen, inferior lateral ventricle, lateral ventricle, third ventricle, fourth ventricle, and CSF values were observed in individuals diagnosed with schizophrenia compared to healthy controls. Additionally, specific regional volumetric reductions were identified in key brain regions implicated in cognitive processing, emotional regulation, and motor control. Notably, the study highlights the widespread nature of these alterations, underscoring the multifaceted neuropathological underpinnings of schizophrenia. Understanding these neuroanatomical changes is vital for elucidating the underlying pathophysiological mechanisms of the disorder. It may pave the way for developing targeted therapeutic interventions to alleviate cognitive and functional deficits. Further research exploring the interplay of genetic, developmental, environmental, and neurobiological factors is warranted to deepen our understanding and improve treatment outcomes for individuals affected by schizophrenia.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of the Atatürk University Faculty of Medicine Clinical Researches Ethics Committee (Date: 26.10.2023, Decision No: 18).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors declared no conflicts of interest concerning the authorship and/or publication of this article.

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### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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