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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(4):1304-8

Automated MRI-Based volumetric analysis of basal nuclei in Parkinson's disease: Comparing MRICloud and IBASPM methods

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Received 12 May 2025; Accepted 25 August 2025
Available online 30 November 2025 with doi: 10.5455/medscience.2025.05.125

Abstract

Parkinson's disease (PD) is associated with characteristic structural changes in basal nuclei, most notably the substantia nigra. While manual segmentation remains the reference standard for volumetric analysis, automated tools offer greater scalability and efficiency. To compare the volumetric measurements of basal nuclei between Parkinson's disease patients and healthy controls using two fully automated segmentation methods—MRICloud and IBASPM. In this retrospective study, 43 PD patients and 45 control participants underwent high-resolution MRI. Volumetric analyses of the caudate nucleus, putamen, globus pallidus, and substantia nigra were conducted using MRICloud and IBASPM. MRICloud identified significantly increased caudate nucleus volumes in PD patients compared to controls. IBASPM showed no significant volumetric differences. Substantia nigra volumes did not differ significantly between groups. Weak inter-method correlations were observed. Automated segmentation tools produce divergent results in basal nuclei volumetry. MRICloud may detect subtle changes in PD more sensitively than IBASPM. Methodological differences must be considered when interpreting automated neuroimaging data.

Keywords: Magnetic resonance imaging, parkinson's disease, basal nuclei, IBASPM, MRICloud

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, primarily affecting the dopaminergic neurons of the substantia nigra pars compacta. The resulting dopamine deficiency leads to the classical motor symptoms of PD, including bradykinesia, rigidity, and resting tremor [1-4]. However, the diagnosis of PD continues to rely largely on clinical criteria due to the absence of a definitive biomarker [2,3,5]. Advances in neuroimaging have enabled the exploration of structural brain changes in PD. Among these, MRI-based volumetric analysis provides a non-invasive approach for quantitatively assessing subcortical structures, including the basal nuclei (BN)—the caudate nucleus (CN), putamen, globus pallidus (GP), and substantia nigra (SN). Previous studies suggest that the SN is one of the earliest and most affected regions in PD pathology [6-8].

While manual segmentation remains the gold standard for volumetric studies, it is time-consuming and operator-dependent. Automated segmentation tools such as MRICloud and IBASPM provide scalable alternatives for large datasets. MRICloud is based on a multi-atlas label fusion framework combined with Large Deformation Diffeomorphic Metric Mapping, enabling parcellation of the brain into more than 250 anatomical units and allowing for highly detailed subcortical analyses. This fully

CITATION
Karakoyun ZN, Oz N, Acer N, et al. Automated MRI-Based volumetric analysis of basal nuclei in Parkinson's disease: comparing MRICloud and IBASPM methods. Med Science. 2025;14(4):1304-8.

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DOI: 10.5455/medscience.2025.05.125

automated method is freely accessible to the public through the MRICloud platform. In contrast, IBASPM is an atlas-based segmentation toolbox integrated into the Statistical Parametric Mapping framework. It employs the Automated Anatomical Labeling atlas and performs segmentation by spatially normalizing individual MR images to a standard anatomical template, followed by inverse mapping of atlas labels to the native space. While this approach makes IBASPM accessible and suitable for broader volumetric analyses, its reliance on a limited atlas may restrict its sensitivity to subtle volumetric differences in small subcortical structures [9,10]. Nevertheless, their comparative accuracy in evaluating BN volumes in PD patients remains underexplored.

This study aims to fill this gap by retrospectively comparing the volumetric measurements of basal nuclei in patients with PD and healthy controls using two automated methods—MRICloud and IBASPM—with a specific focus on the substantia nigra. By evaluating their performance, this research contributes to the development of imaging-based biomarkers and supports the clinical implementation of automated volumetric assessment tools in PD.

Material and Methods

Study Design and Participants

This retrospective study was conducted at the Neurology Department of Akdeniz University Hospital and approved by the Akdeniz University Faculty of Medicine Ethics Committee (Date: 01.11.2017, Protocol No: 646). The study adhered to the principles of the Declaration of Helsinki. Medical records and high-resolution T1-weighted brain MRI scans of 132 patients with suspected PD, obtained between November 2015 and October 2017, were reviewed retrospectively. Inclusion criteria were: (i) a clinical diagnosis of idiopathic PD by a movement disorders specialist, (ii) age ≥ 40 years, and (iii) availability of a high-quality MRI dataset suitable for volumetric analysis.

Exclusion criteria were: (i) atypical Parkinsonian syndromes (e.g., progressive supranuclear palsy, multiple system atrophy), (ii) secondary Parkinsonism, (iii) other neurodegenerative or structural brain diseases (e.g., stroke, hydrocephalus, tumor), (iv) history of brain surgery or deep brain stimulation, (v) MRI artifacts compromising volumetric analysis.

Among the 132 patients, 89 were excluded for the following reasons: 28 had non-idiopathic parkinsonian syndromes (e.g., multiple system atrophy, progressive supranuclear palsy, drug-induced parkinsonism, vascular parkinsonism), 22 had significant comorbid central nervous system pathologies such as infarcts, tumors, or hydrocephalus detected on MRI, 19 had a history of intracranial surgery or deep brain stimulation, and 20 were excluded due to poor image quality resulting from motion or susceptibility artifacts. After exclusions, 43 patients with idiopathic Parkinson's disease who fulfilled all inclusion criteria were included in the final analysis.

The control group (n=45) consisted of individuals who underwent brain MRI due to mild neurological complaints (e.g., headache, vertigo, forgetfulness), but were evaluated as neurologically normal by neurologists. Individuals with history of central nervous system disease, surgery, or major psychiatric disorder were excluded. No age- or sex-matching was applied, but group characteristics were analyzed and adjusted statistically.

Magnetic resonance imaging procedure and image acquisition

All scans were performed using a 3T MRI scanner (Spectra, Siemens Healthcare, Erlangen, Germany). A standardized T1-weighted 3D MPRAGE sequence was used (TR=1900 ms, TE=2.41 ms, flip angle=9°, voxel size=1 mm^3). The acquisition time was 3 min 21 sec.

All MRI scans were originally acquired for routine clinical evaluation but followed a standardized protocol suitable for retrospective volumetric analysis.

Volume estimation techniques

High-resolution T1-weighted images were analyzed using two automated segmentation pipelines:

MRICloud (Johns Hopkins University, Baltimore, MD, USA; https://mricloud.org): A web-based tool employing multi-atlas likelihood fusion. The pipeline includes preprocessing (bias correction, skull stripping), segmentation using Johns Hopkins University's multi-atlas inventories (286 ROIs), and quality control steps based on ontology-level parcellation.

IBASPM toolbox (originally developed at Universidad Complutense de Madrid, Spain; http://www.thomaskoenig.ch/Lester/ibaspm.htm): An SPM-based toolbox using the Automated Anatomical Labeling (AAL) atlas. Segmentations were conducted using SPM5 in MATLAB 7.10, generating 69 subcortical and cortical volumes per scan. Preprocessing included normalization to MNI space and tissue classification.

Notably, MRICloud and IBASPM operate independently, and although both use statistical parametric mapping approaches, they differ in preprocessing, segmentation resolution, and anatomical labeling protocols. The SN was assessable only with MRICloud, while the subthalamic nucleus could be measured only with IBASPM.

Statistical analysis

Statistical analyses were conducted using SPSS software, version 22.0 (IBM Corp., Armonk, NY, USA). A p value less than 0.05 was considered statistically significant. Descriptive statistics, including mean, standard deviation and minimum-maximum values, were calculated for the volume results obtained from MRICloud service and IBASPM software in the PD patient and control groups.

To compare the BN volumes between PD and control groups, the Mann-Whitney U test was applied. Within-subject comparisons between the two methods (MRICloud vs IBASPM) were analyzed using the Wilcoxon signed-rank test. The Chi-square test was used to assess differences in categorical demographic

DOI: 10.5455/medscience.2025.05.125

variables. No imputation was performed for missing data; only complete cases were included in the analyses.

To address selection bias, strict inclusion/exclusion criteria and quality controls were applied. No formal sample size calculation was performed due to the retrospective design.

Results

A total of 43 patients diagnosed with PD (30 men and 13 women; mean age: 65.9±12.4 years) and 45 controls (16 men and 29 women; mean age: 60.3±7.3 years) were included in the analysis. It is important to note that due to the retrospective nature of the study, the control group was not specifically matched for gender and age with each individual PD patient. However, age and sex distributions between groups were evaluated and are summarized in Table 1.

Basal nuclei volumes

The mean volumetry of the right and left BN was assessed using both the MRICloud and IBASPM methods (results presented in Table 2). The volume of the SN was exclusively quantified using the MRICloud service, while the subthalamic nucleus volume was exclusively measured with the IBASPM software. Due to a substantial number of zero results, the subthalamic nucleus volume was excluded from the study.

Comparing the BN volumes obtained through the MRICloud method between the patient and control groups (Table 2), a statistically significant elevation in both the right (p=0.02) and left (p=0.03) CN volumes were observed in individuals with PD. However, no significant differences were found in the other measurement results (p>0.05). Conversely, when comparing the volumes of the BN obtained through the IBASPM method (Table 2) between the patient and control groups, no statistically significant differences were identified (p>0.05) between the two groups.

Comparison of volume results obtained with MRICloud service and IBASPM software

Statistical analyses revealed significant differences in the volumes measured by the MRICloud and IBASPM methods between the patient group and control group (excluding the left CN in the control group) (Table 2). However, no significant relationship was observed between these volumes. Furthermore, the measurements obtained with the MRICloud method were found to be higher than those obtained with the IBASPM method.

Regarding the volumes measured by the MRICloud and IBASPM methods, no significant correlation was found between the left GP, right CN, and left CN volumes in PD patients, as well as the right GP, left GP, and right CN volumes in the control group.

Significant mean differences were observed between the two methods in both the PD and control groups. Notably, a weak positive correlation was identified between the volume measurements of the right and left putamen in PD patients, as measured by the MRICloud and IBASPM methods. Similarly, a weak positive correlation was observed between the left CN volume measurements in the control group (Table 2).

Table 1. Demographic data of patients with PD and healthy control subjects

Demographic characteristics	Patients with PD	Healthy control subjects	p *
Number of subjects	43	45	
Men/women	30/13	16/29	0.01*
Percentage (Men/women)	69.8/30.2	35.6/64.4	
Age mean	65.88 ± 12.38	60.33 ± 7.28	0.01*
Age min/max	40-88	49-78	

*:Chi-square test; p < 0.05 was considered statistically significant; PD: Parkinson's Disease

Table 2. Right and left basal nuclei volumes measured with the MRICloud and IBASPM

Basal nuclei	Methods					
	MRICloud			IBASPM		
	PD (mm^3)	C (mm^3)	p value*	PD (mm^3)	C (mm^3)	p value*
GP-R	1419±193	1386±158	0.39	272±318	266±274	0.93
GP-L	1346±201	1356±178	0.8	154±231	124±222	0.54
CN-R	3481±458	3249±406	0.02	2362±842	2574±587	0.17
CN-L	3381±456	3165±417	0.03	2823±743	3041±480	0.11
Put-R	3955±499	3989±427	0.73	3402±590	3379±520	0.85
Put-L	3758±460	3685±324	0.39	3402±590	3401±470	0.92
SN-R	226±39	226±40	0.99	NA	NA	NA
SN-L	316±48	308±38	0.4	NA	NA	NA

*: Mann Whitney U test; SN: Substantia Nigra; CN: Caudate Nucleus; GP: Globus Pallidus; Put: Putamen; R: Right; C: Control; L: Left; PD: Parkinson's Disease NA: not available

DOI: 10.5455/medscience.2025.05.125

Discussion

This study provides a comparative evaluation of two fully automated MRI-based volumetric tools—MRICloud and IBASPM—in assessing basal nuclei volumes in patients with PD. The main finding was that the MRICloud method revealed significantly larger volumes in the CN of PD patients compared to controls, whereas IBASPM did not detect any statistically significant differences in BN volumes between the groups. These findings underscore the variability between segmentation platforms and the importance of method selection in neuroimaging studies.

The caudate nucleus plays a central role in motor and cognitive functions and is among the basal nuclei often affected in PD. While some studies report a reduction in CN and putamen volumes in PD patients [5,11], our observation of increased CN volume using MRICloud may reflect methodological differences or even early compensatory mechanisms in dopaminergic circuits. Previous literature demonstrates conflicting findings regarding CN volumes in PD, suggesting that results can vary depending on disease stage, patient population, or the imaging software used [7,11]. Several factors may account for this discrepancy. First, methodological considerations must be acknowledged, as atlas-based automated segmentation platforms such as MRICloud may be prone to over-segmentation, particularly in subcortical regions with complex anatomical boundaries. Second, the retrospective design of our study precluded precise information on disease duration or stage, which are known to influence structural trajectories in PD. Finally, it is conceivable that neurobiological compensatory mechanisms occurring during the early phases of the disease may transiently contribute to relative increases in subcortical volumes before overt atrophy becomes detectable. Taken together, these issues highlight the need for cautious interpretation of volumetric findings and for future longitudinal studies integrating both clinical staging and multi-software validation approaches.

The disparity between the findings of MRICloud and IBASPM highlights the importance of understanding the underlying algorithms and segmentation pipelines of each tool. MRICloud employs multi-atlas likelihood fusion with a larger set of anatomical labels [9], which may contribute to its tendency to produce higher volume estimates. In contrast, IBASPM relies on a simpler statistical model and fewer regions of interest [10], potentially limiting its sensitivity in subtle volumetric distinctions. These platform-specific characteristics are crucial when interpreting results and making cross-study comparisons.

Another critical region examined in this study was the SN, known to undergo dopaminergic neuronal loss in PD. While our study did not find significant volume differences in SN between groups using MRICloud, this may be due to technical limitations of automated tools in segmenting small and anatomically complex structures such as the SN. Manual segmentation remains more accurate for such regions [12], although it is resource-intensive and less feasible in large-scale studies. Further advances in image resolution and algorithmic refinement are needed to improve the detection of subtle SN changes using automated pipelines [7,13].

The inability of IBASPM to quantify the subthalamic nucleus (STN) in most subjects represents another methodological limitation. STN is a structure of growing clinical interest, particularly in the context of deep brain stimulation (DBS), and future segmentation software should prioritize the accurate delineation of this nucleus. Similarly, other tools like FreeSurfer or FSL-FIRST, which offer broader and more detailed segmentation capabilities, might be better suited for such assessments [13,14]. Comparing multiple automated pipelines in the same dataset would enhance the robustness and generalizability of volumetric findings in PD research.

Beyond methodology, the clinical utility of automated volumetric analysis tools remains a crucial consideration. As neuroimaging evolves toward personalized medicine, reproducible and scalable tools like MRICloud and IBASPM may facilitate earlier diagnosis and more precise monitoring of neurodegenerative changes in PD [3,9]. However, their implementation in clinical workflows must be tempered with an awareness of their respective limitations, particularly in the context of small or overlapping anatomical structures.

Limitations

This study has several limitations. First, its retrospective design may introduce selection bias. Second, the absence of age and sex matching between PD and control groups raises the possibility of residual confounding, despite statistical adjustments. Third, clinical data such as disease duration, motor symptom severity, or response to treatment were not available, limiting the ability to correlate imaging findings with disease phenotype or progression. Fourth, the inability to evaluate the subthalamic nucleus and the technical constraints in assessing the substantia nigra reduce the comprehensiveness of the volumetric comparison.

From a methodological perspective, only two automated segmentation tools (MRICloud and IBASPM) were included, and broader comparisons with additional platforms would provide a more complete perspective. Another limitation is that the original MRICloud analyses were conducted in 2018, and due to the platform's data retention policy, the segmentation outputs are no longer available for download. While the raw MRI data remain accessible, reprocessing them with updated software versions could generate different results, potentially introducing inconsistencies. For this reason, no new visualizations were generated to preserve methodological fidelity to the original analyses.

Finally, segmentation error probabilities of automated pipelines such as MRICloud and IBASPM cannot be directly assessed with conventional reliability metrics (e.g., inter-rater or test–retest reliability). Potential methodological biases remain, including dependence on atlas selection, reduced sensitivity to subtle volumetric alterations in small nuclei, and decreased accuracy in

DOI: 10.5455/medscience.2025.05.125

pathological brains where deviations from normative templates may occur. These issues should be considered when interpreting the current findings.

Conclusion

This study demonstrates that methodological differences between automated segmentation tools can lead to divergent volumetric estimates in Parkinson's disease, particularly for the caudate nucleus. Only MRICloud identified significant differences between patients and controls, highlighting the need for cautious interpretation of automated data. The lack of significant findings in the substantia nigra and other nuclei suggests current tools may have limited sensitivity for small subcortical structures. Nevertheless, their scalability makes them valuable for research and clinical use, and future studies should combine multi-software comparisons with clinical data to improve diagnostic utility.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

This study was supported by Akdeniz University Scientific Research Projects Coordination Unit (BAP). Project Number: TTU-2018-3240.

Ethical Approval

The Akdeniz University Faculty of Medicine Ethics Committee (Date: 01.11.2017, Protocol No: 646). The study adhered to the principles of the Declaration of Helsinki.

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