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Original Article

Assessment of Asymmetry in Thalamic Nuclei volume in Nigerian Parkinson's Disease Patients

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ABSTRACT

Background and aim: Emerging evidence suggests that asymmetrical alterations in thalamic gray matter may represent a key neuroanatomical feature of Parkinson's disease (PD). However, the expression of these structural changes remains underexplored within African populations. This study examines thalamic asymmetry in a Nigerian cohort of PD patients, aiming to elucidate population-specific patterns of neurodegeneration and their relationship to sociodemographic variables.
Methodology: Twenty-two individuals diagnosed with PD and thirty-four age-matched healthy controls were recruited. Participant demographics, including age, socioeconomic status (SES), and educational attainment, were documented in accordance with Committee on Best Practice in Data Analysis and Sharing (COBIDAS) guidelines. High-resolution T1-weighted MRI scans were acquired using a 1.5T system and processed via FSL_Anat, with thalamic nuclei segmented and volumetrically assessed using FreeSurfer version 7.3.2. Group comparisons were conducted using independent t-tests, while correlational analyses assessed associations between thalamic volumes and age, SES, and education levels.
Results: The present study shows symmetry in the Thalamic nuclei of Parkinson's Disease patients as no significant differences were observed between the left and right thalamic nuclei (P>0.05). There was also interhemispheric symmetry of the thalamic nuclei observed in the control subjects except in the Pc nuclei (p=0.0094).The correlation analysis analysing association between the thalamic nuclei volume and the demographics of the data subjects showed significant asymmetry in the Ventral Anterior magnocellular (VAmc) nucleus of the thalamus among Parkinson's disease (PD) patients, with a p-value of 0.038, indicating a notable lateralization in this motor-related subregion. Additionally, we observed that female patients exhibited reduced VAmc asymmetry compared to males (p = 0.012), highlighting a sex-specific pattern in thalamic structural alterations associated with PD.
Conclusion: These findings advance our understanding of PD-associated thalamic reorganization within an understudied population and underscore the relevance of sociodemographic factors in shaping subcortical brain morphology.

Keywords:
Parkinson's disease, Volumetric Assessment, Thalamic nuclei, Nigerians.

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder closely associated with aging, typically manifesting between the fourth and seventh decades of life (Pang *et al.,* 2022). Clinically, PD presents with hallmark motor symptoms—including tremor, muscular rigidity, bradykinesia, and postural instability—as well as a range of non-motor manifestations (Poewe *et al.,* 2017; Papagno and Trojano, 2018). A distinguishing feature of PD is its unilateral onset, with motor impairments typically emerging on one side of the body before generalizing.

These clinical features are attributed to disruptions in basal ganglia-thalamo-cortical motor circuits, wherein the thalamus plays a central role by relaying and integrating inputs from the cortex, striatum, and pallidum. This degeneration impairs motor control, sensory processing, and broader signal integration, emphasizing the thalamus's involvement in PD pathophysiology (Djaldetti *et al.*, 2006).

Anatomically, the thalamus is a paired gray matter structure located deep within the brain, functioning as a critical hub for motor coordination, sensory perception, and higher-order cognitive activities. Beyond these roles, the thalamus also regulates arousal, attention, and sleep (Whyte *et al.*, 2024). Comprising approximately 60 distinct nuclei (Cassel & de Vasconcelos, 2015), it receives and processes inputs from both the motor cortex and subcortical regions, such as the basal ganglia and cerebellum (Bosch-Bouju *et al*., 2013; Middleton & Strick, 2000).

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Neurodegenerative processes often manifest as brain atrophy, detectable via structural MRI. MRI facilitates the segmentation of the brain into anatomically relevant regions, allowing for the assessment of regional gray matter changes. This imaging modality has proven effective in identifying neuroanatomical alterations in PD and distinguishing it from other neurological disorders (Mahlknecht *et al*., 2010). Notably, thalamic atrophy has emerged as a potential biomarker in PD (Halliday, 2009).

The concept of brain asymmetry, first highlighted in early studies on language lateralization and split-brain phenomena (Broca, 1861; Wernicke, 1874; Sperry, 1961), is now recognized as a key feature of neurodegenerative conditions such as Parkinson's disease (PD), which often presents with asymmetric clinical symptoms. Structural brain changes in PD, particularly in the thalamus, have been shown to align with symptom laterality, including contralateral atrophy in the VIM nucleus (Kassubek *et al.*, 2002) and persistent hemispheric asymmetries in deep brain stimulation outcomes (Pahwa *et al.,* 2006). Borghammer's SOC model attributes this asymmetry to the uneven spread of α-synuclein pathology, implicating the thalamus in both motor and non-motor features of PD. Volumetric and morphometric studies support these observations, reporting bilateral thalamic volume changes associated with disease progression (Geevarghese *et al.,* 2015), hemispheric shape differences (McKeown *et al.,* 2008), and subtype-specific atrophy patterns, particularly in PD patients with REM sleep behavior disorder or cognitive impairment (Salsone *et al.,* 2014; Danti *et al.,* 2015). These findings underscore the relevance of thalamic asymmetry as a potential biomarker for PD heterogeneity.

Despite consistent evidence of asymmetry in PD symptomatology and structure, the role of the thalamus remains inadequately characterized. Given its integrative role in the basal ganglia-thalamo-cortical loop—critical for motor, behavioral, and cognitive functions—thalamic degeneration may contribute substantially to hemispheric asymmetries observed in PD. Understanding asymmetric thalamic atrophy could offer valuable insights into the mechanisms underlying disease progression and cognitive decline. This study focuses on evaluating thalamic volume asymmetry in individuals with PD, with an emphasis on identifying hemispheric differences in structural alterations. By investigating these changes in an African cohort, the study also aims to broaden our understanding of PD neuropathology across diverse populations.

MATERIALS AND METHODS

Ethical Approval

Ethical approval was obtained from the Research Ethics Committee of the University Of Port-Harcourt, Nigeria with the reference code: UPH/CERMAD/REC/MM84/056.

Neuroimaging data sources: Data were collected from three Neuroimaging Diagnostic centers in Nigeria from three centers; two centers (RSUTH lab, and the Intercontinental Lab) are located in Port Harcourt, South-Southern part of Nigeria, while one center (the LifeBridge Diagnostic Lab) is in Abuja, North –Central part of Nigeria.

Study participants: Participants or their guardians signed informed consent forms for data collection for diagnostic and research purposes. Participants were not financially compensated for participation. A total of 88 MRI anatomical sequences were collected across 56 Nigerian participants, all of whom originate and also reside in Nigeria. Due to the sensitive nature of the data, and to protect the confidentiality and privacy of the subjects, data protection measures such as pseudonymization (defacing, manual brain masking), dedicated access control procedures, and Data Use Agreements (DUA), were developed and utilized. In total, the dataset is comprised of 42 PD participants with age 57.5 ± 30.41 for male and 61.0 ± 24.04 for female expressed in Mean±SD and a range of 25-75 years and 40 healthy control participants with ages 50.0 ± 35.36 for male and 61.0 ± 24.04 For female expressed in Mean±SD and a range of 36-79 years. Children, teenagers, non Nigerians and participants with metallic implants and pacemakers were excluded from the study. The brain MRI of one of the recruited participants from the control group was removed from this study to achieve a closely matched age group between the control and the PD patients. Only healthy participants were accepted for the study. We accepted only participants who could give informed consent. Participants must be Nigerian citizens. We accepted only participants with no major neurological disorder Table 1 below, provides a breakdown of the demographics of the participant groups.

Table 1: Demographics of study participants.

Clinical group	Sex	Number of subjects	Age range(years)	Mean(years)± Standard deviation
Control	M	27	25-75	50.0 ± 35.36
	F	13	25-56	40.5 ± 21.92
PD	M	26	36-79	57.5 ± 30.41
	F	15	48-78	61.0 ± 24.04

Below, we follow the COBIDAS reporting protocol (Nicholas *et al.,* 2017) to describe subjects' information, exclusion, and inclusion criteria, and socioeconomic status (SES) information. SES was measured using a combination of income, class, and education, consistent with best practices for SES indicators (Antonoplis, 2022). Specifically, we categorized the individuals into upper, middle, and lower class based on their economic standing, likely reflecting both income and occupation. Additionally, their highest level of education (e.g., completed tertiary, secondary, or informal education) was recorded.

Sex Distribution: 64% of the Parkinson subjects were males while 36% of them were females. For the healthy control group, 69% are males, while 31% are females.

Socioeconomic Status (SES) distribution: Among the Parkinson patients, 18% have lower SES distribution, 45% are Middle class while 5% are Upper class 5%, 32% provided no information on their SES. For the healthy control group, 23% belong to the lower class, 69% belongs to the middle class and 8% belongs to the upper class

Education Distribution: For Parkinson subjects, 0% had informal education, 59% had Secondary education while 41% had Tertiary education. Among the healthy control subjects, 20% have informal education, 46% have secondary education and 34% have tertiary education.

Neuroimaging parameters. Participant data from the RSUTH lab were collected using a GE Signa 1.5T (Software version SV25.1_R04_1743.a and SV25.1_R07_2127.a) scanner, whereas data from the LifeBridge Diagnostic Lab were collected using a Toshiba MRT200PP3 1.5T scanner (Software version V9.51*R249), and data from the Intercontinental lab were collected using a Hitachi AIRIS II 0.3T scanner (Software version V5.1H-1). A 12-channel head coil was used at all sites. For a subset of participants, multiple runs of data collection were performed (i.e. run-1, run-2, run-3, run-4). For a larger subset contrast-enhanced T1w images were collected, where the contrast agent used was gadolinium. Due to the unique data acquisition parameters, not all participants have the same number of images. The type of data orientation, contrast enhancement, or run can be different across subjects. Information regarding the breakdowns of the number of images collected across the various acquisition parameters is reported in Wogu et al., 2025.

Anatomical data (T1w) Pre-processing: The raw data contain anatomical (T1-weighted) sequences. These DICOMs were converted to BIDS using ezBIDS (Levitas *et al*., 2024).

Anatomical MRI Quality Metrics Assessment: Upon conversion, the NIfTI images were visually inspected using FSL's slicer functionality (Woolrich *et al.,* 2009; Smith, *et al.*, 2004; Jenkinson *et al.,* 2012) implemented in brainlife.app.300, brainlife.app.301, and brainlife.app.689.

Following this, quality metrics of the T1w images were computed using MRIQC (Esteban et al., 2017) in brainlife.app.701 and brainlife.app.702.

The mean CNR for the T1-weighted MRI scan of both the Parkinson's Disease patients and the healthy controls as calculated by MRIQC, was 3.5 (range: 3.0-4.0). This indicates good image quality with good contrast between gray and white matter.

To prevent visual identification of study participants, the T1-weighted images were defaced using mri_deface(http://www.na-mic.org/Wiki/index.php/Mbirn:_Defacer_for_structural_MR) (Gorgolewski et al., 2013). The defaced T1w datasets were imputed into the brainlife.io platform(defaced_datasets). To crop, reorient, and debiase the images to match the orientation of the MNI152 template, the fsl_anat (T1) process on Brainlife was staged and executed. The cropped and reoriented images were then linearly aligned using FMRIB's Linear Image Registration Tool (FLIRT) and subsequently aligned non-linearly to the MNI152 1mm template using FNIRT (Greve and Fischl, 2009). The linearly aligned images will hereafter be referred to as the 'acpc aligned' anatomical (T1w) images. The non-linearly aligned image, often referred to as the "warped" image, underwent a more complex transformation compared to the linear alignment process. This transformation involves adjusting the image to better match the intricate anatomical features of a standard template, such as the MNI152 1mm template mentioned. This involved techniques like nonlinear registration or deformation-based morphometry. These techniques allow for more flexible adjustments to align the individual anatomical features of the subject's brain with those of the template. After the non-linear alignment process, the resulting image is usually referred to as the "registered" or "warped" image. This image represents the subject's anatomical data in a standardized space, allowing for more accurate comparisons and analyses across different subjects.

Anatomical Image processing (thalamic nuclei segmentation)

Following alignment, the 'acpc aligned' anatomical (T1w) images were processed using Freesurfer 7.3.2. This software was used to evaluate the volume of thalamic subregions by generating a parcellation of the thalamus into 25 different nuclei, using a probabilistic atlas built with histological data. The parcellation is based on structural MRI, either the main T1 scan processed through recon-all [http://freesurfer.net/fswiki/ThalamicNuclei] Subsequently, Freesurfer Statistics was used to convert important parcellation statistics, including volume to a .csv file for each hemisphere. The output data for the respective thalamic nuclei was used for the statistical analysis.

Asymmetry Index (AI) Assessment: The AI is a widely used measure in brain asymmetry studies (Kurth, *et al.,* 2015; Leroy *et al.,* 2015). To ascertain if there is asymmetry or symmetry between the left and right hemispheres of the thalamic nuclei, we quantified thalamic asymmetry Index (AI) (Kong *et al.,* 2022) using the formula below;

AI= (Left – Right)/(Left + Right).

This formula only calculates the asymmetry index for each person in the PD and healthy controls but since our goal in this study is to carry out an inter-group study to answer these questions, "Is there asymmetric difference in the thalamic nuclei between PD patients and healthy controls?", "How much is the difference?", "Is the difference statistically significant?". To answer these questions we used a regression model — not just the formula.

After calculating the AI, we fit in a Mixed Linear Model (MixedLM) which generates the β- coefficient (which tells us about the size of the group difference) and p-value (which tells us whether the difference is significant or not). The β-coefficient is the value of estimated percentage increase in the thalamic nucleus interhemispheric asymmetry in Parkinson's patients Vs the control. Positive β values indicate greater leftward asymmetry in

Parkinson's patients; negative β values indicate greater rightward asymmetry.

Statistical Analysis

The thalamic nuclei volumes were expressed in Means ± Standard Deviation and the statistical analysis were performed using Python, specifically leveraging the pandas, statsmodels, seaborn, and matplotlib libraries in a Jupyter Notebook environment. To compare the thalamic nuclei volumes between the PD patients and the healthy controls, an independent t-test was used.

We employed a linear mixed-effects regression to quantify how demographic (age, sex, education) and socioeconomic (SES) factors—and Parkinson's versus control status—independently influence thalamic asymmetry while correctly modeling the fact that each subject contributes 26 correlated measurements (one per nucleus). By including a subject-level random intercept, the model captures each individual's baseline asymmetry and thus accounts for within-person correlation, avoiding the inflated Type I error that would arise under a simple ordinary-least-squares approach. Fixed effects for centered age, sex, education level, SES, diagnostic group, nucleus identity, and the group×nucleus interaction then estimate, in a single coherent framework, both overall and region-specific shifts in asymmetry. Model parameters were obtained by maximum likelihood in Python's statsmodels, residuals were inspected for normality and homoscedasticity, multicollinearity was ruled out via variance-inflation factors, and false-discovery-rate correction was applied across nuclei, yielding unbiased, efficient inferences about how clinical and sociodemographic factors shape thalamic asymmetry in Parkinson's disease.The analyses were performed using Python, specifically leveraging the pandas, statsmodels, seaborn, and matplotlib libraries in a Jupyter Notebook environment. To visualize the regression findings, a forest plot-style figure was generated to illustrate the standardized beta coefficients and their 95% confidence intervals for each predictor across nuclei.

RESULTS

Findings from the present study reveal a uniform absence of statistically significant left–right volume differences in the PD group for all twenty-six subnuclei. Mean volumes in the left and right hemispheres were closely matched— for example, the mediodorsal magnocellular nucleus (MDm) measured 677.44 ± 128.86 mm^3 on the left versus 647.03 ± 114.69 mm^3 on the right (p = 0.486), and the pulvinar medial (PuM) measured 1,137.25 ± 220.16 mm^3 versus 1,109.43 ± 207.05 mm^3 (p = 0.715). Across the board, p-values exceeded the 0.05 threshold, indicating that any asymmetry, if present, falls below our detection limit given sample size and measurement variability. In contrast, the healthy control cohort displayed a single small but statistically significant asymmetry in the parvocellular nucleus (Pc), with right-hemisphere volume slightly exceeding left (4.24 ± 0.84 mm^3 vs. 3.81 ± 0.58 mm^3, p = 0.0094). No other nuclei in controls reached significance.

To ascertain group differences in thalamic asymmetry indices, β coefficients was generated from mixed-effects regression comparing Parkinson's patients to controls. Positive β values indicate greater leftward asymmetry in Parkinson's patients; negative β values indicate greater rightward asymmetry. The β-coefficient depicts the value of estimated percentage increase in the thalamic nucleus interhemispheric asymmetry in Parkinson's patients Vs the control. The findings show an estimated 5.8-percentage-point increase in VAmc interhemispheric asymmetry compared to controls. The VAmc stands out with β = 0.0584 (p = 0.038), reflecting an average AI increase of +0.0313 in PD patients. In contrast, other nuclei showed much smaller or even negative shifts—e.g. the centrolateral (CL) nucleus +0.0720, lateral posterior (LP) +0.0388, laterodorsal (LD) +0.0387, and lateral geniculate (LGN) +0.0323, versus medial geniculate (MGN) –0.0324 and pulvinar lateral (PuL) –0.0168—none of which approached statistical significance (all p > 0.1), underscoring the unique asymmetrical remodeling of VAmc in Parkinson's disease.

Each dot shows how much more (or less) asymmetric a nucleus is in PD patients versus controls, and each horizontal line is the 95% confidence interval. Only the VAmc nucleus's interval lies entirely to the right of zero, indicating a significant shift.

In our mixed-effects regression of asymmetry indices (AI) across all 26 thalamic nuclei, only the ventral anterior magnocellular (VAmc) nucleus emerged as a robust locus of PD-related lateralization. Controlling for age, sex, socioeconomic status, and education, Parkinson's disease status predicted an increase in VAmc AI (β = 0.0584, p = 0.038) as shown figure 2, the boxplot of VAmc Asymmetry Index (AI) by group, with the full model explaining 17.9 % of the variance in VAmc asymmetry (R^2 = 0.179). In practical terms, PD patients showed, on average, a 5.8 percentage-point greater left->right volume difference in VAmc than controls, indicating a subtle but reliable shift in subnuclear geometry (Oltra *et al.,* 2022).

The Boxplot visually summarizes the shift in median and spread that underlies the observed group effect (β = 0.0584, p = 0.038). This implies that the Parkinson's Disease patients shows an estimated 5.8-percentage point increase in the Vamc nuclei asymmetry when compared to the control.

Figure 4 presents a global segmentation overlay that highlights only the entire thalamic mask (in green) alongside surrounding structures, without showing subnuclear boundaries. This broad visualization was used to verify the accuracy of AC–PC alignment and FreeSurfer segmentation across all subjects before extracting nucleus-specific volumes. In future work, incorporating an atlas overlay with distinct color-coding for each nucleus (e.g., CM, VM, Pt, VAmc, VPL, VLp) would more clearly delineate their precise anatomical boundaries and visually link each significant volumetric change to its respective subregion.

Assessment of thalamic nuclei Asymmetry between the left and right hemispheres of the brain of Nigerian Parkinson's Disease patients and healthy controls

	Parkinson's Disease				Healthy Control			
Thalamic Nucleus	Left Hemisphere	Right Hemisphere	p-value	Inference	Left Hemisphere	Right Hemisphere	p-value	Inference
AV	168.40±51.67	172.88±48.68	0.8024	Not significant	147.43±40.86	157.05±43.56	0.3117	Not Significant
CL	59.93±24.18	53.05±19.86	0.3854	Not Significant	50.70±22.37	52.17 ± 20.75	0.7618	Not Significant
CM	349.32±76.69	326.99±67.50	0.3887	Not Significant	286.37±54.99	276.05±51.08	0.3868	Not Significant
CeM	88.00±25.83	83.88 ± 25.52	0.6530	Not Significant	80.41 ± 21.18	81.76 ± 24.05	0.7895	Not Significant
L-Sg	36.11±12.81	32.90 ± 15.66	0.5298	Not Significant	32.18 ± 14.90	28.55 ± 10.85	0.2173	Not Significant
LD	39.16±21.84	36.86 ± 21.56	0.7659	Not Significant	36.86 ± 19.69	37.90 ± 20.61	0.8171	Not Significant
LGN	272.78±67.40	231.72±64.57	0.0880	Not Significant	271.56 ± 79.35	248.92 ± 61.69	0.1585	Not Significant
LP	125.72±36.85	117.30±41.79	0.5495	Not Significant	130.06 ± 35.42	128.27 ± 43.35	0.8402	Not Significant
MDl	252.01±73.97	240.75±54.88	0.6284	Not Significant	268.79 ± 60.62	262.60 ± 58.69	0.6441	Not Significant
MDm	677.44±128.86	647.03±114.69	0.4859	Not Significant	717.66 ± 113.00	695.05 ± 132.14	0.4135	Not Significant
MGN	102.39±25.91	112.27±33.65	0.3594	Not Significant	105.60 ± 33.40	109.27 ± 40.76	0.6608	Not Significant
MV(Re)	18.85±7.77	17.88 ± 8.59	0.7406	Not Significant	18.12 ± 7.98	17.80 ± 8.49	0.8621	Not Significant
Pc	4.12±0.83	4.30 ± 0.84	0.5669	Not Significant	3.81 ± 0.58	4.24 ± 0.84	0.0094	Significant
Pf	76.75±18.37	76.02 ± 18.04	0.9104	Not Significant	66.60 ± 17.69	68.95 ± 17.09	0.5475	Not Significant
Pt	10.39±2.63	9.99 ± 2.15	0.6450	Not Significant	8.30 ± 2.12	8.36 ± 1.93	0.8877	Not Significant
PuA	206.15±41.76	195.31 ± 38.38	0.4502	Not Significant	215.84 ± 40.67	210.65 ± 39.57	0.5642	Not Significant
PuI	300.54±82.29	280.66 ± 69.44	0.4658	Not Significant	292.55 ± 70.24	285.52 ± 63.25	0.6394	Not Significant
PuL	240.25±66.52	233.80±51.08	0.7606	Not Significant	230.79±55.51	222.15±61.11	0.5098	Not Significant
PuM	1137.25±220.16	1109.43±207.05	0.7152	Not Significant	1151.46±213.91	1152.55±176.22	0.9802	Not Significant
VA	453.04±84.74	433.82±93.43	0.5465	Not Significant	423.56±71.28	423.16±101.19	0.9839	Not Significant
VAmc	42.83±8.30	40.34±8.27	0.4024	Not Significant	35.61±7.09	36.21±8.12	0.7230	Not Significant
VLa	722.94±111.31	708.93±133.47	0.7492	Not Significant	645.09±88.78	648.94±130.04	0.8777	Not Significant
VLp	944.90±147.66	925.35±156.46	0.7186	Not Significant	839.71±115.03	835.82±164.60	0.9028	Not Significant
VM	27.28±5.05	26.00±4.99	0.4759	Not Significant	22.96±4.54	22.28±4.93	0.5215	Not Significant
VPL	976.95±191.27	947.63±163.00	0.6439	Not Significant	855.00±118.07	839.18±160.98	0.6176	Not Significant

P<0.05 = significant

AV, anteroventral; LD, laterodorsal; LP, lateral posterior; VA, ventral anterior; VAmc, ventral anterior magnocellular; VLa, ventral lateral anterior; VLp, ventral lateral posterior; VPL, ventral posterolateral; VM, ventromedial; CeM, central medial, CL, central lateral; Pc, paracentral; CM, centromedian; Pf, parafascicular; Pt, paratenial; MV-re, medial ventral reuniens; MDm, mediodorsal medial magnocellular; MDl, mediodorsal lateral parvocellular; LGN, lateral geniculate; MGN, medial geniculate; L-Sg, limitans supragenicuiate; PuA, pulvinar anterior; PuM, pulvinar medial; PuL, pulvinar lateral; PuI, pulvinar Inferior;

Figure 2: Assessment of Asymmetry Index using statistical regression (MixedLM Model).

Nucleus	Mean Asymmetric Index (AI)	β-Coefficient (Parkinson – Control)	p-value
AV	–0.0222	0	0.8024
CL	0.0049	0.072	0.3854
CM	0.0203	–0.0223	0.3887
CeM	0.0095	0.0041	0.653
L-Sg	0.0534	0.0072	0.5298
LD	–0.0077	0.0163	0.7659
LGN	0.051	0.0395	0.088
LP	0.0246	0.0089	0.5495
MDl	0.0091	0.0096	0.6284
MDm	0.0171	0.0304	0.4859
MGN	–0.0260	–0.0324	0.3594
MV(Re)	0.0246	0.0053	0.7406
Pc	–0.0369	0.0183	0.5669
Pf	–0.0116	–0.0093	0.9104
Pt	0.0002	0.0081	0.645
PuA	0.014	–0.0108	0.4502
PuI	0.0183	–0.0235	0.4658
PuL	0.0151	–0.0168	0.7606
PuM	0.0006	0.0139	0.7152
VA	0.0136	–0.0192	0.5465
VAmc	0.0088	0.0584	0.038
VLa	0.0039	–0.0146	0.7492
VLp	0.0053	–0.0196	0.7186
VM	0.0163	–0.0172	0.4759
VPL	0.0077	–0.0291	0.6439

AV, anteroventral; LD, laterodorsal; LP, lateral posterior; VA, ventral anterior; VAmc, ventral anterior magnocellular; VLa, ventral lateral anterior; VLp, ventral lateral posterior; VPL, ventral posterolateral; VM, ventromedial; CeM, central medial, CL, central lateral; Pc, paracentral; CM, centromedian; Pf, parafascicular; Pt, paratenial; MV-re, medial ventral reuniens; MDm, mediodorsal medial magnocellular; MDl, mediodorsal lateral parvocellular; LGN, lateral geniculate; MGN, medial geniculate; L-Sg, limitans suprageniculate; PuA, pulvinar anterior; PuM, pulvinar medial; PuL, pulvinar lateral; PuI, pulvinar Inferior;

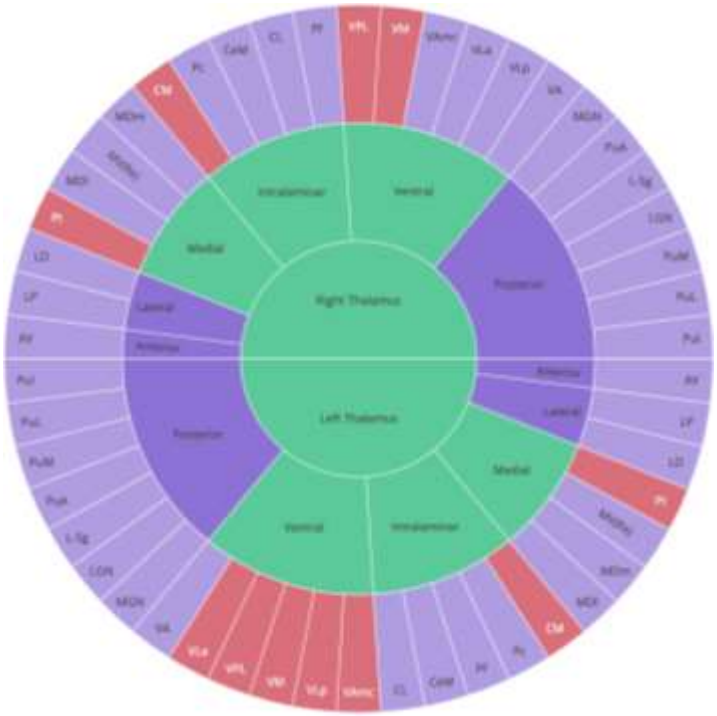

Figure 1. Radial Visualization of Thalamic Nuclei Volumes in Nigerian PD patients - This interactive sunburst plot displays the PD mean volumes of various thalamic nuclei, organized hierarchically by hemisphere (left/right), functional region (e.g., Ventral, Intralaminar), and individual nucleus. The slice sizes correspond to the PD volumes, and the colors indicate statistical significance (crimson for significant and medium-purple for not significant).

Associations between thalamic nuclei volumes and age, SES, and education levels.

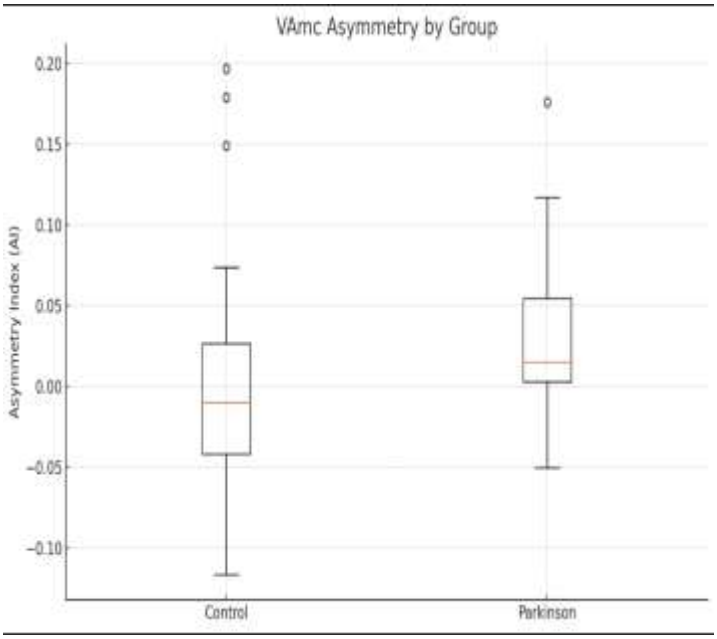

Figure 2: Boxplot for the regression analysis of VAmc Asymmetry Index (AI) by group (Control vs. Parkinson),

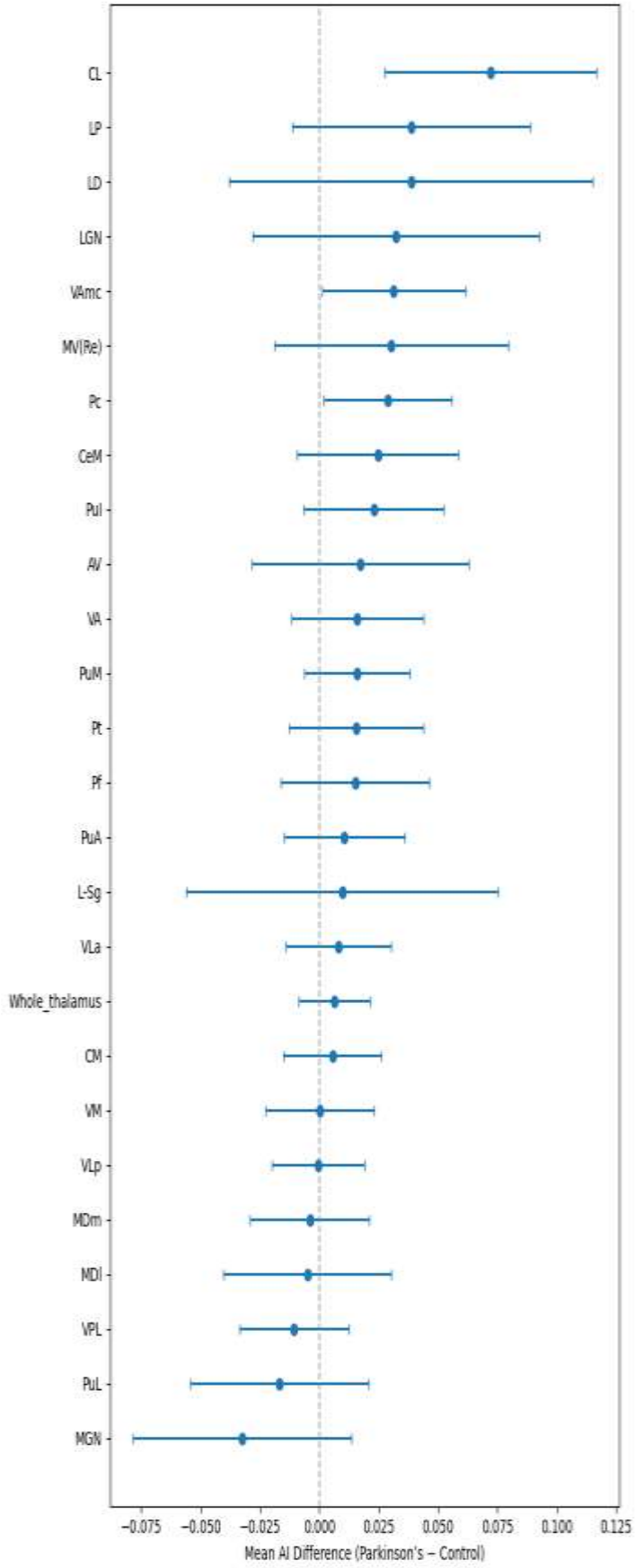

Figure 3. Forest plot of Parkinson's effect on thalamic asymmetry.

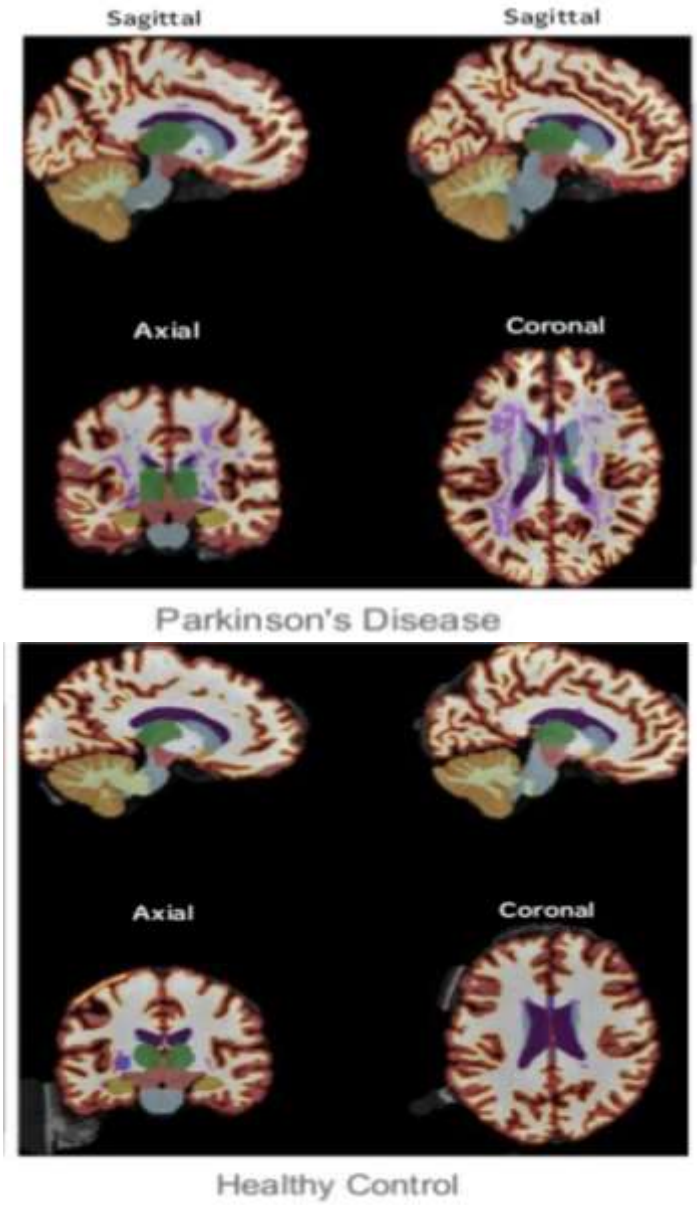

Figure 4: Showing the thalamus in Parkinson's disease (left panels) versus healthy control (right panels) using Freesurfer 7.3.2. The brain structures are color-coded, with the thalamus itself highlighted in green. Panels show sagittal views (top row), coronal view (bottom left), and axial view (bottom right).

DISCUSSION

In this study, we performed a comprehensive survey of interhemispheric gray-matter volumes across twenty-six thalamic subnuclei in a cohort of Nigerian Parkinson's disease (PD) patients and age-matched healthy controls. The thalamus serves as a critical relay station for both sensorimotor and higher-order cognitive circuits (Sheridan and Tadi 2023; Brazhnik *et al.,* 2016; Li *et al.,* 2025) and asymmetric degeneration of its subregions has been implicated in the lateralization of motor symptoms and non-motor deficits in PD (Chen *et al.,* 2023; Fan *et al.,* 2019; Faria *et al.,* 2023; Hansen *et al.,* 2025). However, most prior investigations

have been limited to a handful of major nuclei. By extending our analysis to include all anatomically defined thalamic subnuclei—ranging from the anterior ventral (AV) and centromedian (CM) groups through the parvocellular (Pc) division and ventrolateral (VL) complex—we sought to determine whether lateralized atrophy is a widespread feature of thalamic involvement in PD, or whether degeneration occurs more symmetrically in this under-studied population.

The complete symmetry observed in PD patients suggests that, within this Nigerian sample, thalamic degeneration proceeds in a bilaterally parallel fashion rather than targeting one hemisphere preferentially. This finding diverges from several European-centered studies (Steinbach *et al*., 2021; Li *et al.,* 2020; Liang and Mendell, 2013;Lin *et al*., 2013:) that have reported mild lateralization—such as left-dominant atrophy in early-stage PD (Zhang *et al.,* 2023) or right-dominant changes in more advanced cases. Such discrepancies may arise from ethnic or genetic factors influencing disease expression, differences in MRI acquisition or segmentation protocols, or variation in disease duration and severity. Our cross-sectional design cannot disentangle these possibilities, but it does underscore the importance of including diverse populations in neurodegenerative research.

The normative asymmetry in the Pc nucleus among controls aligns with established functional lateralization in thalamic relay pathways (Starkey *et al.,* 2023); the parvocellular division participates in fine sensory discrimination and visual processing, functions known to exhibit hemispheric specialization. That this asymmetry does not appear in PD patients may reflect a disease-related attenuation of normal lateralization, perhaps due to uniform neuronal loss or compensatory reorganization that equalizes volumes. Alternatively, the small absolute size of the Pc nucleus increases measurement variability, and the lack of significant asymmetry in PD could stem from reduced statistical power in this tiny structure.

Our study carries several limitations. Although analyzing twenty-six nuclei represents a more granular approach than most prior work, the modest sample size limits sensitivity to detect subtle asymmetries, particularly in smaller subnuclei. Moreover, volumetric segmentation of diminutive regions such as Pc or the reticular MV(Re) nucleus is technically challenging, and residual segmentation errors may obscure true differences. The cross-sectional nature precludes assessment of how asymmetry evolves over time or in relation to clinical milestones such as onset of motor complications or cognitive decline. Future investigations should incorporate longitudinal imaging, larger cohorts, and multimodal measures (e.g. diffusion metrics, functional connectivity) to more fully characterize lateralized thalamic pathology and its clinical correlates.

Beyond disease status, **biological sex** also shaped VAmc asymmetry, being female was associated with **–0.0504 lower Asymmetric Index (p = 0.012)**, a roughly 5 percentage-point reduction in lateralization compared to males. This suggests that in women—even with PD present—the VAmc remains more symmetrical than in men. No other covariates (age, SES, education) reached significance in the VAmc model, nor did PD status predict asymmetry in any other thalamic subregion (Oltra *et al.,* 2022).

The specificity of this finding to the VAmc division dovetails with its known role in motor-related thalamocortical circuits. VAmc sits in the anterior motor relay zone, channeling basal ganglia output into the premotor cortex—precisely the pathway most implicated in PD's hallmark unilateral motor onset. An elevated AI here likely reflects compensatory hypertrophy or uneven neurodegeneration contralateral to the clinically more affected side (Lanciego *et al.,* 2012).

That no other nuclei showed significant group effects underlines a selective vulnerability of the VAmc subregion to PD-associated asymmetry. While the intralaminar centromedian (CM) nucleus and medial paratenial (Pt) nucleus exhibited volumetric changes in the raw t-tests, only the VAmc asymmetry survived the multivariable regression. This reinforces the idea that asymmetry—and not just atrophy—may be the more sensitive marker of PD-specific thalamic remodeling (Lee *et al*., 2011) .

Additionally, when visualized as a forest plot of nucleus-specific Group β estimates as shown in figure 3, the VAmc stands out with β = 0.0584 (p = 0.038), reflecting an average AI increase of +0.0313 in PD patients. In contrast, other nuclei showed much smaller or even negative shifts—e.g. the centrolateral (CL) nucleus +0.0720, lateral posterior (LP) +0.0388, laterodorsal (LD) +0.0387, and lateral geniculate (LGN) +0.0323, versus medial geniculate (MGN) –0.0324 and pulvinar lateral (PuL) –0.0168—none of which approached statistical significance (all p > 0.1), underscoring the unique asymmetrical remodeling of VAmc in Parkinson's disease(Mai and Majtanik, 2019).

In contrast, the paracentral (Pc) nucleus may appear to lie at a similar position, but its confidence interval overlaps zero (and its p > 0.05), so it does not reach statistical significance once age, sex, SES, education, and multiple comparisons are accounted for.

Our model's modest R^2 (0.179) reminds us that VAmc asymmetry is only one piece of the PD neuropathology puzzle. Longitudinal studies will be needed to map how this lateralization evolves with disease progression, and whether it correlates with contralateral symptom severity or response to unilateral deep-brain stimulation. Nevertheless, the combination of a significant PD-effect, a clear sex difference, and the centrality of VAmc in motor circuits makes this finding a compelling candidate biomarker for asymmetrical thalamic reorganization in Nigerian Parkinson's disease patients.

In Figure 1's radial chart, the VAmc slice in the ventral-motor ring is the only subregion whose adjusted asymmetry (β = 0.0584, p = 0.038) remains significant in our regression analysis, highlighting its vulnerability to lateralized neurodegeneration in Parkinson's disease. This is consistent with Lanciego *et al.* (2012), who described the VAmc as a key relay in the motor thalamocortical loop, where asymmetrical dysfunction could reflect the typically unilateral onset of PD motor symptoms. In contrast, the Pc

nucleus within the intralaminar-sensory ring showed significant asymmetry only in the healthy control group (p = 0.0094), possibly reflecting normal lateralization in sensory processing. This aligns with the findings of Starkey *et al.* (2023), who reported conserved thalamic lateralization patterns in sensory circuits, which may be disrupted or equalized in Parkinson's due to uniform neurodegeneration.

Conclusion: This study provides a comprehensive analysis of thalamic asymmetry in Nigerian Parkinson's disease patients, revealing a largely symmetrical pattern across subnuclei, except for the ventral anterior magnocellular (VAmc) nucleus, which exhibited a significant leftward asymmetry specific to PD. This supports the hypothesis that thalamic reorganization in Parkinson's may be regionally selective and influenced by disease laterality, particularly within motor-related circuits. Additionally, the paracentral (Pc) nucleus showed normal asymmetry in healthy controls, suggesting that PD may attenuate otherwise typical patterns of thalamic lateralization. These findings highlight the VAmc as a potential subcortical biomarker for asymmetrical neurodegeneration in PD and shows the importance of population-specific imaging studies in understanding disease expression across diverse cohorts.

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