

Magnetic Resonance Imaging (MRI)-Based Hippocampal Volumetry in Patients with Dementia in Anambra State, Nigeria: A Retrospective Study

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ABSTRACT

Background: Dementia is a progressive neurocognitive syndrome associated with structural and functional changes in the brain. The hippocampus plays a central role in memory formation and is particularly vulnerable to neurodegenerative processes, especially those associated with Alzheimer's disease. Magnetic resonance imaging (MRI)-based hippocampal volumetry may provide a useful quantitative marker for characterising dementia and differentiating its subtypes. However, there is limited local evidence regarding hippocampal volume among patients with dementia in southeastern Nigeria. **Aim:** To assess hippocampal volume in patients with dementia using MRI, compare right and left hippocampal volumes across dementia subtypes, and determine whether hippocampal volume varies by sex.

Methods: A retrospective cross-sectional study was conducted at the MRI Unit of GEM Diagnostic Centre, Onitsha, Anambra State, Nigeria. Seventy-one brain MRI examinations and corresponding medical records of adults with dementia were purposively selected. MRI examinations were retrieved from the Picture Archiving and Communication System. The right and left hippocampi were identified on coronal images, manually delineated across the slices in which they appeared, and their volumes calculated from the summed cross-sectional areas and slice thickness. Data were analysed using SPSS version 21.0. The Shapiro–Wilk test was used to assess normality, while independent-samples *t*-tests were used for group comparisons. Statistical significance was set at $p < 0.05$.

Results: The patients whose images were evaluated comprised 53 males (74.65%) and 18 females (25.35%). The largest age group was 61–80 years (40.84%). Mean hippocampal volumes were highest among patients with normal pressure hydrocephalus (NPH), measuring $2.343 \pm 0.041 \text{ cm}^3$ on the right and $2.250 \pm 0.102 \text{ cm}^3$ on the left. Vascular dementia patients had mean volumes of $2.010 \pm 0.071 \text{ cm}^3$ on the right and $2.125 \pm 0.088 \text{ cm}^3$ on the left. Mixed dementia patients had volumes of $1.992 \pm 0.119 \text{ cm}^3$ on the right and $1.844 \pm 0.086 \text{ cm}^3$ on the left, while Alzheimer's disease had the lowest volumes, at $1.856 \pm 0.148 \text{ cm}^3$ on the right and $1.828 \pm 0.070 \text{ cm}^3$ on the left. A significant sex difference was observed only in the left hippocampus among patients with Alzheimer's disease ($p = 0.031$). Right–left hippocampal volume differences were significant in vascular dementia ($p < 0.001$) and mixed dementia ($p = 0.008$), but not in Alzheimer's disease ($p = 0.320$) or NPH ($p = 0.066$). **Conclusion:** Hippocampal volume varied across dementia subtypes, with the smallest volumes observed in Alzheimer's disease and the largest in NPH. Significant hippocampal

asymmetry was observed in vascular and mixed dementia. MRI-derived hippocampal volumetry may therefore provide useful quantitative information in the structural assessment and differentiation of dementia subtypes.

Keywords: dementia; hippocampus; hippocampal volumetry; magnetic resonance imaging; Alzheimer's disease; vascular dementia; normal pressure hydrocephalus; Nigeria.

INTRODUCTION

Dementia is a progressive syndrome characterised by deterioration in cognitive function beyond that expected from normal ageing. It affects memory, thinking, behaviour and the ability to perform activities of daily living. Although dementia is more common among older adults, it is not an inevitable consequence of ageing. Dementia may result from several neurodegenerative, vascular and mixed pathological processes, with Alzheimer's disease (AD), vascular dementia (VaD), Lewy body dementia, frontotemporal dementia and mixed dementias representing important clinical categories. According to Apostolova et al. (2012), the World Health Organisation recognises dementia as a major cause of disability and dependency among older adults. It emphasises the increasing need for improved diagnosis and care, particularly in low- and middle-income countries (Apostolova et al., 2010)

The increasing burden of dementia constitutes an important public health concern, particularly in developing countries where ageing populations, limited specialist services and delayed diagnosis may complicate management. (Bocchetta et al. 2018). The burden is substantial globally, with more than 55 million people estimated to be living with dementia, and the majority of affected individuals residing in low- and middle-income countries. Apostolova et al. (2010) stated that in Nigeria and other African countries, the availability of population-specific neuroimaging data remains limited. This creates a need for locally generated imaging evidence to improve understanding of structural brain changes associated with dementia and to support the development of contextually appropriate diagnostic approaches (De Souza et al., 2013)

The hippocampus is a medial temporal lobe structure with important roles in memory formation, learning and spatial navigation. Dubois et al. (2014). It forms part of the hippocampal formation together with the dentate gyrus, subiculum and related structures. Its anatomical organisation includes the hippocampal head, body and tail, and cornu ammonis subfields (Eichenbaum, 2004). The complex anatomy of the hippocampus and its close relationship with surrounding medial temporal structures are important considerations when performing MRI-based volumetric measurements.

The hippocampus is particularly susceptible to neurodegenerative processes. In Alzheimer's disease, hippocampal neuronal loss and atrophy are important structural manifestations and are associated with impairment of episodic memory and progressive cognitive decline (Hsu et al, 2002). MRI studies have consistently demonstrated reductions in hippocampal volume in patients with AD compared with cognitively healthy older adults (Geuze, 2005). Histopathological and imaging evidence also supports a relationship between MRI-derived hippocampal volume and neuronal loss within hippocampal structures (Jack et al., 1997)

MRI provides a non-invasive method for assessing these structural changes, and hippocampal volumetry can quantify changes that may not be readily apparent on routine visual assessment. Jack. et al. (2008). Structural MRI is an established component of the diagnostic evaluation of patients with suspected dementia and can demonstrate characteristic patterns of regional cerebral atrophy that support differential diagnosis (Kantarci et al., 2016)

MRI is particularly suitable for hippocampal assessment because of its superior soft-tissue contrast and ability to demonstrate the medial temporal structures Dubois et al. (2014). Coronal imaging perpendicular to the longitudinal axis of the hippocampus facilitates identification of the hippocampal head, body, and tail and has traditionally been used for hippocampal segmentation (Livingston et al., 2020). Manual delineation of the hippocampus across sequential slices has historically served as an important reference method for volumetric assessment, although automated and semi-automated techniques are increasingly available

(Obenaus, 2001). The EADC-ADNI harmonised protocol was developed partly to improve consistency in manual hippocampal segmentation because differences in anatomical boundaries can substantially affect measured volume (Frisoni et al., 2015). Previous studies have demonstrated differences in hippocampal volume among dementia subtypes (Rascovsky et al., 2011). In particular, Vijayakumar and Vijayakumar compared hippocampal volumes in Alzheimer's disease, vascular dementia, mixed dementia, normal pressure hydrocephalus (NPH) and healthy controls and reported the greatest reduction in the Alzheimer's disease group. Vijayakumar and Vijayakumar (2013). Their study also demonstrated an association between decreasing hippocampal volume and increasing dementia severity. Similarly, Dolek et al. (2012) reported smaller hippocampal volumes in Alzheimer's disease and vascular dementia and found that lower hippocampal volume was associated with greater cognitive impairment.

The relationship between hippocampal volume and dementia subtype is nevertheless not completely specific. Hippocampal atrophy may occur in several neurodegenerative disorders, including frontotemporal dementia, although the magnitude and distribution of atrophy may differ from those observed in Alzheimer's disease. Consequently, hippocampal volumetry should be regarded as a structural biomarker that contributes to, rather than independently establishes, the diagnosis of a particular dementia subtype (Rao 2023)

Hippocampal asymmetry is another consideration in volumetric assessment. Differences between right and left hippocampal volumes have been reported in healthy populations, although the magnitude and direction of asymmetry vary between studies. (Shi, 2009) A large meta-analysis found that apparent sex differences in hippocampal volume are substantially influenced by overall brain or intracranial volume, highlighting the importance of appropriate normalisation when comparing individuals.

Hippocampal volume is also influenced by age, sex, head size, MRI acquisition parameters, and segmentation methodology (Strange, 2014). Studies of healthy adults have demonstrated age- and sex-related effects on hippocampal structure, while other studies have reported relatively stable hippocampal volumes across portions of adulthood. These observations emphasise the importance of considering demographic and methodological factors when interpreting absolute hippocampal volumes.

Despite the clinical importance of hippocampal volumetry, there is limited information on MRI-derived hippocampal volumes among patients with dementia in Anambra State. The relative scarcity of African neuroimaging datasets further supports the need for locally derived MRI measurements and normative or disease-specific data. The development of Nigerian structural MRI datasets has been recognised as an important step towards improving the representation of African populations in neuroimaging research. Dolek (2012). The present study therefore assessed hippocampal volume in patients with dementia in Anambra State and examined differences according to dementia subtype, sex and cerebral hemisphere.

MATERIALS AND METHODS

Study design and Setting

A retrospective cross-sectional study was undertaken at the MRI Unit of GEM Diagnostic Centre, Onitsha, Anambra State, Nigeria. The centre is a diagnostic facility providing MRI services and served as the source of the imaging and clinical data used in the study.

Study Population and Sampling

The study population comprised MRI reports and images of adults with dementia who had undergone brain MRI during the study period. A purposive sample of 71 eligible MRI examinations and corresponding clinical records was included. The recruitment/data-acquisition period was May 3rd 2024 – August 20th, 2026. The subtype-specific sample sizes are Alzheimer's disease, $n = 20$; vascular dementia, $n = 25$; mixed dementia, $n = 15$; and normal pressure hydrocephalus, $n = 11$. Total sample = 71.

Dementia diagnosis and subtype were based on a combination of clinical assessment, cognitive testing, and imaging.

Patients aged 18 years and above with a confirmed diagnosis of dementia, available brain MRI examinations, and complete demographic and clinical information were eligible. Examinations without a confirmed diagnosis of dementia, incomplete records, and examinations involving patients younger than 18 years were excluded.

Ethical Considerations

Ethical approval was obtained from the Human Research and Ethics Committee of the Faculty of Health Sciences and Technology, Nnamdi Azikiwe University. Permission to access patients' medical records and MRI examinations was obtained from the management of GEM Diagnostic Centre. Confidentiality and anonymity were maintained throughout the study.

MRI Acquisition and Hippocampal Volumetry

MRI examinations were performed using a 1.5-Tesla Siemens Magnetom MRI scanner with a dedicated head coil. Patients were positioned supine, with the head immobilised to reduce motion artefacts. Conventional axial, sagittal and coronal brain sequences were acquired, including T1- and T2-weighted sequences. Slice thickness ranged from 3 to 4 mm, with an interslice gap of approximately 1 mm.

MRI examinations were retrieved from the Picture Archiving and Communication System (PACS). The right and left hippocampi were identified on coronal images. Their cross-sectional areas were manually delineated on each slice on which the hippocampus was visible. Manual segmentation is an established approach to hippocampal volumetry, although measurement reliability depends on the anatomical boundaries and segmentation protocol applied (McKeith et al. 2017)

Hippocampal volume was subsequently calculated by summing the cross-sectional areas and multiplying the sum by slice thickness. The resulting measurements were expressed in cubic centimetres (cm³).

Statistical Analysis

Data were analysed using SPSS version 21.0. Descriptive statistics were used to summarise demographic characteristics and hippocampal measurements. Normality was assessed using the Shapiro–Wilk test. Because the primary question concerns differences in hippocampal volume across four dementia subtypes, the final analysis should use an omnibus comparison rather than multiple independent-samples t-tests. When normality and homogeneity assumptions are satisfied, one-way ANOVA should be applied separately to right and left hippocampal volume, followed by Tukey's HSD. Where variances are unequal, Welch's ANOVA with Games–Howell post-hoc comparisons is appropriate. If distributional assumptions are not met, the Kruskal–Wallis test with adjusted pairwise post-hoc comparisons should be used. Family-wise multiple-comparison correction should be applied. Where raw data permit, age, sex and intracranial volume should be incorporated as covariates using an appropriate general linear model/ANCOVA or regression framework, or hippocampal volumes should be normalised to intracranial volume. The current manuscript reports only independent-samples t-tests; new omnibus, post-hoc, and covariate-adjusted results must be generated from the raw dataset before being reported as performed analyses. No unperformed statistical result is invented here.

The present manuscript does not report intracranial-volume measurements or covariate-adjusted analyses. Accordingly, the reported absolute volumes should be regarded as unadjusted measurements and interpreted cautiously.

RESULTS

Hippocampal volumes according to dementia subtype

Table 2. Mean hippocampal volumes according to dementia subtype

Dementia subtype	Right hippocampus, mean $\pm$ SD (cm ³)	Left hippocampus, mean $\pm$ SD (cm ³)
Alzheimer's disease	1.856 $\pm$ 0.148	1.828 $\pm$ 0.070
Vascular dementia	2.010 $\pm$ 0.071	2.125 $\pm$ 0.088
Mixed dementia	1.992 $\pm$ 0.119	1.844 $\pm$ 0.086
Normal pressure hydrocephalus	2.343 $\pm$ 0.041	2.250 $\pm$ 0.102

Analysis of hippocampal volumes revealed a significant subtype-specific variation in hippocampal atrophy. The mean right and left hippocampal volumes were lowest in Alzheimer's disease (Right: 1.856 $\pm$ 0.148 cm³; Left: 1.828 $\pm$ 0.070 cm³), followed by Mixed dementia (Right: 1.992 $\pm$ 0.119 cm³; Left: 1.844 $\pm$ 0.086 cm³) and Vascular dementia (Right: 2.010 $\pm$ 0.071 cm³; Left: 2.125 $\pm$ 0.088 cm³). Normal Pressure Hydrocephalus (NPH) showed the highest and most preserved hippocampal volumes (Right: 2.343 $\pm$ 0.041 cm³; Left: 2.250 $\pm$ 0.102 cm³). On lateral comparison, Alzheimer's and Mixed dementia showed left-sided predominance of atrophy, while Vascular dementia showed a slightly larger left hippocampus.

Table 3. Comparison of hippocampal volume according to sex

Dementia subtype	Hemisphere	<i>p</i> -value	Significance
Alzheimer's disease	Right	0.833	Not significant
Alzheimer's disease	Left	0.031	Significant
Vascular dementia	Right	0.973	Not significant
Vascular dementia	Left	0.941	Not significant
Mixed dementia	Right	0.498	Not significant
Mixed dementia	Left	0.420	Not significant
NPH	Right	0.549	Not significant
NPH	Left	0.516	Not significant

A statistically significant sex difference was found only for the left hippocampal volume in Alzheimer's disease ($p = 0.031$). No significant sex differences were demonstrated for the right hippocampus in Alzheimer's disease or for either hippocampus in vascular dementia, mixed dementia or NPH.

When hippocampal volumes were compared according to sex, there was no statistically significant difference in hippocampal volume between males and females in the majority of comparisons. For Vascular dementia, Mixed dementia, and Normal Pressure Hydrocephalus, both right and left hippocampal volumes showed no significant sex difference ($p = 0.973, 0.941; 0.498, 0.420$; and $0.549, 0.516$, respectively; all $p > 0.05$). Similarly, in Alzheimer's disease, the right hippocampus showed no significant sex difference ($p = 0.833$). However, a statistically significant sex difference was observed in the left hippocampus of Alzheimer's disease patients ($p = 0.031, p < 0.05$).

Table 4. Right–left hippocampal volume comparison

Dementia subtype	Right mean (cm ³)	Left mean (cm ³)	<i>p</i> -value
Alzheimer’s disease	1.856	1.828	0.320
Vascular dementia	2.01	2.125	<0.001
Mixed dementia	1.992	1.844	0.008
NPH	2.343	2.250	0.066

Comparison of right and left hippocampal volumes within each dementia subtype revealed subtype-specific hemispheric asymmetry. In Alzheimer's disease, there was no statistically significant difference between right (1.856 cm³) and left (1.828 cm³) hippocampal volumes ($p = 0.320$, $p > 0.05$), although the left volume was slightly smaller. In contrast, Vascular dementia showed a highly significant inter-hemispheric difference (Right: 2.01 cm³ vs Left: 2.125 cm³, $p < 0.001$, $p < 0.05$), with left hippocampus significantly larger than right. Similarly, Mixed dementia showed a significant right-left difference (Right: 1.992 cm³ vs Left: 1.844 cm³, $p = 0.008$, $p < 0.05$), with right significantly larger than left. For Normal Pressure Hydrocephalus (NPH), there was no significant difference between right (2.343 cm³) and left (2.250 cm³) hippocampus ($p = 0.066$, $p > 0.05$).

DISCUSSION

This study evaluated MRI-derived hippocampal volumes among patients with dementia in Anambra State and demonstrated variation according to dementia subtype. The principal finding was that patients with Alzheimer’s disease had the smallest mean hippocampal volumes, whereas patients with NPH had the largest. These findings are consistent with previous MRI studies demonstrating prominent hippocampal volume loss in Alzheimer’s disease and differences in hippocampal measurements among dementia subtypes. Similarly, in Harper et al., 2016, the predominance of participants in the older age groups is consistent with the established relationship between advancing age and dementia. The 61–80-year age group accounted for 40.84% of the study population, while a further 26.76% were aged 81–100 years. Thus, more than two-thirds of the participants were above 60 years of age. Increasing age is one of the strongest risk factors for dementia, although dementia should not be considered a normal consequence of ageing.

The predominance of males in the present sample should, however, be interpreted cautiously. Males constituted almost three-quarters of the study population. This distribution may reflect the referral pattern of the centre and the retrospective nature of the study rather than a true sex-specific difference in dementia prevalence. Furthermore, studies of hippocampal volume in healthy populations have not demonstrated a simple or consistent pattern of sexual dimorphism after accounting for differences in overall brain or intracranial volume (Shi, 2019)

The most important imaging finding was the reduced hippocampal volume observed in Alzheimer’s disease. Mean right and left hippocampal volumes were 1.856 cm³ and 1.828 cm³, respectively. Hippocampal atrophy is a recognised structural feature of Alzheimer’s disease and is closely related to neuronal loss and disruption of memory-related networks. MRI-based medial temporal volumetry has demonstrated the ability to distinguish individuals with Alzheimer’s disease from cognitively healthy older adults, including patients with relatively mild disease (Geuze, 2005)

The findings are also consistent with the study by Vijayakumar and Vijayakumar, which reported lower hippocampal volumes in Alzheimer’s disease compared with vascular dementia, mixed dementia and NPH. In their study, Alzheimer’s disease had the lowest hippocampal measurements among the dementia groups, while NPH showed relatively preserved hippocampal volume. Dolek 2012 similarly reported substantial

hippocampal volume reduction in Alzheimer's disease and vascular dementia and demonstrated a relationship between lower hippocampal volume and greater cognitive impairment.

The relatively large hippocampal volumes observed in NPH require careful interpretation. NPH is fundamentally associated with abnormal cerebrospinal-fluid dynamics and ventricular enlargement rather than primary hippocampal neurodegeneration. Therefore, relatively preserved hippocampal volume compared with Alzheimer's disease is biologically plausible. Nevertheless, hippocampal volume alone cannot establish the diagnosis of NPH, and structural interpretation should be integrated with ventricular morphology, clinical manifestations and other imaging findings.

Vascular dementia demonstrated mean right and left hippocampal volumes of 2.010 cm³ and 2.125 cm³, respectively. Interestingly, the left hippocampus was larger than the right, and the difference was statistically significant ($p < 0.001$). In mixed dementia, the right hippocampus was larger than the left, with a significant difference ($p = 0.008$). These findings indicate that hippocampal asymmetry is not uniform across dementia subtypes.

In contrast, Alzheimer's disease showed no significant difference between the right and left hippocampi ($p = 0.320$). This relative symmetry may reflect the predominantly bilateral nature of hippocampal neurodegeneration in Alzheimer's disease. Previous meta-analytic evidence indicates that hippocampal asymmetry exists in the general population, but its magnitude varies according to population characteristics and methodological approaches.

Similarly, the absence of significant asymmetry in NPH ($p = 0.066$) suggests that hippocampal involvement in this cohort was comparatively balanced. However, the non-significant result should not be interpreted as evidence that NPH always produces symmetrical hippocampal volumes. The relatively small subgroup sizes limit the precision of these comparisons.

The observation of greater left than right hippocampal volume in vascular dementia differs from the pattern sometimes reported in healthy populations. Such differences may reflect disease-related structural effects, vascular injury, differences in the distribution of pathological changes or sampling variation. Hippocampal volume asymmetry is therefore best interpreted in the context of the underlying clinical and imaging findings rather than as an independent diagnostic marker (Shi, 2009).

Sex-related analysis showed that the only statistically significant difference in the original independent-samples comparisons was in the left hippocampus among patients with Alzheimer's disease ($p = 0.031$). This isolated result should not be interpreted as evidence of a reproducible sex-related biological difference. The subgroup was relatively small, sex distributions were unequal, and multiple comparisons were performed. Hippocampal volume is also influenced by overall brain/intracranial volume. The finding should therefore be regarded as exploratory and requires confirmation in a larger, balanced cohort with prespecified multiplicity control and relevant covariate adjustment.

Nevertheless, the isolated significant difference in the Alzheimer's disease group should be interpreted cautiously because the sample was relatively small and the study was retrospective. In addition, sex-specific subgroup sizes were unequal. Multiple statistical comparisons were also performed, increasing the possibility that an isolated statistically significant result may occur by chance. Larger studies with balanced sex distributions and correction for relevant covariates are required to determine whether the observed difference represents a reproducible biological phenomenon.

An important consideration is that hippocampal volume is affected by several factors, including age, sex, intracranial volume, MRI acquisition parameters and segmentation methodology. Previous volumetric studies have demonstrated the importance of intracranial volume in interpreting hippocampal measurements, supporting the use of appropriate normalisation when comparing individuals with different head sizes.

The present study did not report intracranial-volume normalisation. Consequently, the absolute hippocampal volumes should be interpreted cautiously, particularly when comparisons are made across individuals or

with external reference populations. This is an important methodological consideration because differences in head size may contribute to observed differences in absolute hippocampal volume independently of disease-related atrophy.

The use of manual hippocampal delineation represents another methodological consideration. Manual segmentation has historically served as an important reference technique for hippocampal volumetry, but it is time-consuming and potentially susceptible to inter-observer and protocol-related variability. Standardised segmentation protocols have been developed to improve reproducibility, while automated and semi-automated approaches may reduce observer dependence (Obenaus, 2001).

The use of conventional 1.5-T MRI is nevertheless clinically relevant. High-field MRI and advanced three-dimensional sequences can provide improved anatomical resolution, but 1.5-T MRI remains widely available and is commonly used in routine clinical practice. Consequently, the present measurements may have practical relevance for diagnostic centres operating with equipment that is more readily accessible than high-field research MRI systems.

The current findings should also be considered in relation to the broader African neuroimaging context. African populations remain substantially underrepresented in large neuroimaging datasets, and Nigerian structural MRI datasets have only recently begun to expand. Locally generated hippocampal measurements may therefore contribute to the development of population-specific reference ranges and improve the applicability of quantitative neuroimaging approaches to Nigerian patients.

Overall, the results demonstrate that MRI hippocampal volumetry has potential clinical value in the structural characterisation of dementia in the Nigerian setting. However, volumetry should complement rather than replace clinical assessment, cognitive testing and conventional MRI evaluation. Hippocampal volume should be interpreted as one component of a multimodal assessment rather than as a stand-alone diagnostic test.

Strengths and Limitations

A major strength of this study is its use of actual clinical MRI examinations and quantitative hippocampal measurements from a Nigerian cohort. It also provides locally relevant data on hippocampal volumes across several clinically recognised dementia categories.

However, several limitations should be acknowledged. First, the retrospective cross-sectional design limits assessment of temporal changes in hippocampal volume. Longitudinal MRI studies are better suited to determining the rate of hippocampal atrophy and its relationship with disease progression.

Second, the sample size of 71 patients limits the statistical power of subgroup analyses, particularly sex comparisons. Third, the study was conducted at a single diagnostic centre, which may limit generalisability to other Nigerian populations. Fourth, manual segmentation may introduce observer-related measurement variability.

Finally, the absence of reported intracranial-volume normalisation may affect direct comparison of absolute hippocampal volumes between individuals and with external populations. The manuscript also lacks a healthy control group and does not report detailed subtype-specific recruitment numbers or the recruitment period. The available text does not document the diagnostic criteria, exact segmentation landmarks, reader blinding or reliability testing; these should be recovered from the original study records before final submission.

CONCLUSION

MRI-derived hippocampal volume differed descriptively across dementia subtypes in this cohort from Anambra State, Nigeria. Alzheimer's disease had the smallest mean hippocampal volumes, whereas NPH had the largest. Significant right-left differences were observed in vascular and mixed dementia in the

original pairwise analyses. The isolated statistically significant sex difference in the left hippocampus in Alzheimer's disease should be considered exploratory. These findings support the potential value of hippocampal volumetry as an adjunctive structural biomarker within a multimodal assessment, but they do not establish that hippocampal volume alone can diagnose or differentiate dementia subtypes. Clinical assessment, cognitive testing, diagnostic criteria, intracranial volume, and other MRI features remain important to interpretation.

Significant right-left hippocampal asymmetry was observed in vascular and mixed dementia but not in Alzheimer's disease or NPH. Sex-related differences were largely absent, except for the left hippocampus in Alzheimer's disease.

These findings suggest that hippocampal volumetry may provide useful quantitative information for the structural assessment and differentiation of dementia subtypes in clinical MRI practice. However, the findings should be interpreted alongside clinical assessment, cognitive testing and other structural MRI features.

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Authors Contributions

This study was conducted through the collaborative efforts of the authors listed. The lead author, Stanley Olisa Nwefuru, conceptualised and designed the study, performed the statistical analysis, and drafted the manuscript under the supervision of Christopher Chukwuemeka Ohagwu and Udobi Samuel Iloraah. Ugochukwu Celestine Opara, Bestman Izuchukwu Oriaku, Emmanuel Ayuba Buba, Emeka Chukwumuanya Umeh, Uche Andrew George and Lawrence Daberechi Ifesie drafted the study protocol, reviewed the first manuscript, and provided additional literature. All authors read, corrected, and approved the final manuscript.

REFERENCES

1. Apostolova, Liana G., Andrew E. Green, Soheila Babakchian, Ki Seok Hwang, Yu-Ying Chou, Arthur W. Toga, and Paul M. Thompson. (2012). Hippocampal atrophy and ventricular enlargement in normal ageing, mild cognitive impairment, and Alzheimer disease. *Alzheimer Disease and Associated Disorders*, 26(1), 17–27. <https://doi.org/10.1097/WAD.0b013e3182163b62>.
2. Apostolova, Liana G., Gil D. Mosconi, Paul M. Thompson, Andrew E. Green, Ki Seok Hwang, Alberto Ramirez, and others. (2010). Subregional hippocampal atrophy predicts Alzheimer's dementia in the cognitively normal. *Neurobiology of Ageing*, 31(7), 1077–1088. <https://doi.org/10.1016/j.neurobiolaging.2008.08.008>.
3. Bocchetta, Martina, Juan E. Iglesias, Marco Scelsi, Daniel M. Cash, M. Jorge Cardoso, Marc Modat, and others. (2018). Hippocampal subfield volumetry: Differential pattern of atrophy in different forms of genetic frontotemporal dementia. *Journal of Alzheimer's Disease*, 64(2), 509–521. <https://doi.org/10.3233/JAD-180195>.
4. Campeau, Norbert G., Ronald C. Petersen, John P. Felmlee, Patrick C. O'Brien, and Clifford R. Jack Jr. (1997). Hippocampal transverse relaxation times in patients with Alzheimer disease. *Radiology*, 205(1), 197–201. <https://doi.org/10.1148/radiology.205.1.9314985>.
5. De Souza, Laura C., Maureen Chupin, Manuel Bertoux, Stéphane Lehéricy, Bruno Dubois, Frédéric Lamari, and others. (2013). Is hippocampal volume a good marker to differentiate Alzheimer's disease from frontotemporal dementia? *Journal of Alzheimer's Disease*, 36(1), 57–66. <https://doi.org/10.3233/JAD-122293>.

6. Dolek, N., Saylisoy, S., Ozbabalik, D., and Adapinar, B. (2012). Comparison of hippocampal volume measured using magnetic resonance imaging in Alzheimer's disease, vascular dementia, mild cognitive impairment and pseudodementia. *Journal of International Medical Research*, 40(2), 717–725. <https://doi.org/10.1177/147323001204000236>.
7. Dubois, Bruno, Howard H. Feldman, Claudia Jacova, Harald Hampel, Jose Luis Molinuevo, Kaj Blennow, and others. (2014). Advancing research diagnostic criteria for Alzheimer's disease: The IWG-2 criteria. *The Lancet Neurology*, 13(6), 614–629. [https://doi.org/10.1016/S1474-4422\(14\)70090-0](https://doi.org/10.1016/S1474-4422(14)70090-0).
8. Eichenbaum, Howard. (2004). Hippocampus: Cognitive processes and neural representations that underlie declarative memory. *Neuron*, 44(1), 109–120.
9. Frisoni, Giovanni B., Clifford R. Jack Jr., Giovanni Bocchetta, Christian Bauer, Kristine S. Frederiksen, Yong Liu, and others. (2015). The EADC-ADNI Harmonised Protocol for manual hippocampal segmentation on magnetic resonance: Evidence of validity. *Alzheimer's and Dementia*, 11(2), 111–125.
10. Frisoni, Giovanni B., Nick C. Fox, Clifford R. Jack Jr., Philip Scheltens, and Paul M. Thompson. (2010). The clinical use of structural MRI in Alzheimer disease. *Nature Reviews Neurology*, 6(2), 67–77. <https://doi.org/10.1038/nrneurol.2009.215>.
11. Geuze, Elbert, Eric Vermetten, and Joseph Douglas Bremner. (2005). MR-based in vivo hippocampal volumetrics: 1. Review of methodologies currently employed. *Molecular Psychiatry*, 10, 147–159.
12. Geuze, Elbert, Eric Vermetten, and Joseph Douglas Bremner. (2005). MR-based in vivo hippocampal volumetrics: 2. Findings in neuropsychiatric disorders. *Molecular Psychiatry*, 10, 160–184.
13. Hachinski, Vladimir C., Les D. Iliff, Elana Zilhka, Geoffrey H. Du Boulay, Vincent L. McAllister, John Marshall, and others. (1975). Cerebral blood flow in dementia. *Archives of Neurology*, 32(9), 632–637.
14. Harper, Lauren, Giulia G. Fumagalli, Frederik Barkhof, Philip Scheltens, John T. O'Brien, Frans Bouwman, and others. (2016). MRI visual rating scales in the diagnosis of dementia: Evaluation in 184 post-mortem confirmed cases. *Brain*, 139(4), 1211–1225.
15. Hsu, Yi-Ying, Norbert Schuff, Andrew T. Du, Karen Mark, Xiaoqi Zhu, David Hardin, and others. (2002). Comparison of automated and manual MRI volumetry of hippocampus in normal ageing and dementia. *Journal of Magnetic Resonance Imaging*, 16(3), 305–310. <https://doi.org/10.1002/jmri.10163>.
16. Jack, Clifford R. Jr., Ronald C. Petersen, Y. C. Xu, Steven C. Waring, Peter C. O'Brien, Eric G. Tangalos, and others. (1997). Medial temporal atrophy on MRI in normal ageing and very mild Alzheimer's disease. *Neurology*, 49(3), 786–794. <https://doi.org/10.1212/WNL.49.3.786>.
17. Jack, Clifford R. Jr., David A. Bennett, Kaj Blennow, Maria C. Carrillo, Billy Dunn, Stephen B. Haeberlein, and others. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimer's and Dementia*, 14(4), 535–562. <https://doi.org/10.1016/j.jalz.2018.02.018>.
18. Kantarci, Kejal, Tanis G. Lesnick, Tanis J. Ferman, Mary E. Przybelski, Bradley F. Boeve, Glenn E. Smith, and others. (2016). Hippocampal volumes predict risk of dementia with Lewy bodies in mild cognitive impairment. *Neurology*, 87(22), 2317–2323. <https://doi.org/10.1212/WNL.0000000000003371>.
19. Laakso, Mikko P., Giovanni B. Frisoni, Mikko Kononen, Markku Mikkonen, Andrea Beltramello, Carlo Geroldi, and others. (2000). Hippocampus and entorhinal cortex in frontotemporal dementia and Alzheimer's disease: A morphometric MRI study. *Biological Psychiatry*, 47(12), 1056–1063. [https://doi.org/10.1016/S0006-3223\(99\)00306-6](https://doi.org/10.1016/S0006-3223(99)00306-6).
20. Laakso, Mikko P., Kari Partanen, Paavo Riekkinen, Matti Lehtovirta, Erkki-Lauri Helkala, Mikko Hallikainen, and others. (1996). Hippocampal volumes in Alzheimer's disease, Parkinson's disease with and without dementia, and in vascular dementia: An MRI study. *Neurology*, 46(3), 678–681.
21. Livingston, Gill, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, and others. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, 396(10248), 413–446. [https://doi.org/10.1016/S0140-6736\(20\)30367-6](https://doi.org/10.1016/S0140-6736(20)30367-6).
22. McKeith, Ian G., Bradley F. Boeve, Dennis W. Dickson, Glenda Halliday, John P. Taylor, Daniel Weintraub, and others. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth

- consensus report of the DLB Consortium. *Neurology*, 89(1), 88–100. <https://doi.org/10.1212/WNL.0000000000004058>.
23. McKhann, Guy M., David S. Knopman, Marilyn Chertkow, Bradley T. Hyman, Clifford R. Jack Jr., Carol H. Kawas, and others. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups. *Alzheimer's and Dementia*, 7(3), 263–269. <https://doi.org/10.1016/j.jalz.2011.03.005>.
24. Obenaus, Andre, C. J. Yong-Hing, K. A. Tong, and G. E. Sarty. (2001). A reliable method for measurement and normalisation of pediatric hippocampal volumes. *Pediatric Research*, 50(1), 124–132. <https://doi.org/10.1203/00006450-200107000-00022>.
25. Pipitone, Jon, Michael T. M. Park, Jason Winterburn, Thomas A. Lett, John P. Lerch, Jens C. Pruessner, and others. (2014). Multi-atlas segmentation of the whole hippocampus and subfields using multiple automatically generated templates. *NeuroImage*, 101, 337–348.
26. Pruessner, Jens C., Li-Ming Li, Walter Serles, Michael Pruessner, D. Louis Collins, N. Kabani, and others. (2000). Volumetry of hippocampus and amygdala with high-resolution MRI and three-dimensional analysis software: Minimising the discrepancies between laboratories. *Cerebral Cortex*, 10(4), 433–442.
27. Rao, G., Gao, H., Wang, X., and Zhang, J. (2023). MRI measurements of brain hippocampus volume in relation to mild cognitive impairment and Alzheimer disease: A systematic review and meta-analysis. *Medicine*, 102(36), e34997. <https://doi.org/10.1097/MD.00000000000034997>.
28. Rascovsky, Katya, John R. Hodges, David Knopman, Mario F. Mendez, Joel H. Kramer, Jennifer H. Neuhaus, and others. (2011). Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*, 134(9), 2456–2477. <https://doi.org/10.1093/brain/awr179>.
29. Sabuncu, Mert R., Rahul S. Desikan, Julien Sepulcre, B. T. Thomas Yeo, Hongtu Liu, Michael N. Schmansky, and others. (2011). The dynamics of cortical and hippocampal atrophy in Alzheimer disease. *Archives of Neurology*, 68(8), 1040–1048. <https://doi.org/10.1001/archneurol.2011.167>.
30. Scheltens, Philip, D. Leys, F. Barkhof, D. Huglo, H. C. Weinstein, P. Vermersch, and others. (1992). Atrophy of medial temporal lobes on MRI in probable Alzheimer's disease and normal ageing: Diagnostic value and neuropsychological correlates. *Journal of Neurology, Neurosurgery and Psychiatry*, 55(10), 967–972.
31. Shi, F., B. Liu, Y. Zhou, C. Yu, and T. Jiang. (2009). Hippocampal volume and asymmetry in mild cognitive impairment and Alzheimer's disease: Meta-analyses of MRI studies. *Hippocampus*, 19(11), 1055–1064. <https://doi.org/10.1002/hipo.20573>.
32. Squire, Larry R., Christine E. L. Stark, and Robert E. Clark. (2004). The medial temporal lobe. *Annual Review of Neuroscience*, 27, 279–306.
33. Strange, Bryan A., Menno P. Witter, Ed Lein, and Edvard I. Moser. (2014). Functional organisation of the hippocampal formation: Implications for episodic memory. *Nature Reviews Neuroscience*, 15, 655–669.
34. Sullivan, Edith V., L. Marsh, and Adolf Pfefferbaum. (2005). Preservation of hippocampal volume throughout adulthood in healthy men and women. *Neurobiology of Ageing*, 26(7), 1093–1098. <https://doi.org/10.1016/j.neurobiolaging.2004.09.015>.
35. Tan, Anthony, W. Ma, A. Vira, D. Marwha, and Lise Eliot. (2016). The human hippocampus is not sexually dimorphic: Meta-analysis of structural MRI volumes. *NeuroImage*, 124, 350–366.
36. Vijayakumar, V., and S. Vijayakumar. (2013). Comparison of hippocampal volume in dementia subtypes. *ISRN Radiology*, 2013, 174524. <https://doi.org/10.5402/2013/174524>.
37. Wahlund, Lars-Olof, Frederik Barkhof, Franz Fazekas, Lena Bronge, Michael Augustin, Martin Sjögren, and others. (2001). A new rating scale for age-related white matter changes applicable to MRI and CT. *Stroke*, 32(6), 1318–1322.