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Correlation Between Diabetes Mellitus and Quantitative Brain Volumetric Changes in Patients with Dementia: An Ambispective Cohort Study Using AI-Based MRI Volumetry.

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Abstract

Background: Diabetes mellitus (DM) is associated with cognitive impairment and structural brain abnormalities. However, its relationship with quantitative brain volume in patients with established dementia remains uncertain. AI-based automated MRI volumetry provides objective assessment of regional brain volume loss. Aim: To determine whether laboratory-confirmed DM is associated with quantitative brain volume changes in patients with dementia using AI-based MRI volumetry. ***Methods***: An ambispective observational cohort study included 100 patients with dementia identified from institutional records. MRI volumetric parameters, including global cerebral gray and white matter (GWM) volume loss, cerebral cortex (CC) volume loss, and right and left hippocampal atrophy (HA), were retrieved from existing reports. DM was classified using fasting plasma glucose and/or HbA1c according to ADA criteria. Between-group comparisons, Pearson correlation, and age-adjusted ANCOVA were performed. ***Results***: Of 100 patients (mean age 73.48 ± 10.54 years), 64 (64.0%) were DM-positive and 36 (36.0%) DM-negative. GWM volume loss was significantly higher in DM-positive patients (789.42 ± 60.89 vs 747.94 ± 105.49 mm^3; p = 0.035) and remained significant after age adjustment (p = 0.014). CC volume loss was also higher in DM-positive patients (435.64 ± 33.84 vs 415.36 ± 57.31 mm^2) and remained significant after adjustment (p = 0.022). No significant associations were observed with right or left hippocampal measurements. ***Conclusion***: DM was independently associated with greater GWM and CC volume loss, but not hippocampal atrophy, suggesting a region-specific relationship between DM and brain structural changes in dementia.

Keywords: Diabetes mellitus; dementia; brain volumetry; MRI; artificial intelligence; cerebral cortex; hippocampus.

INTRODUCTION

Dementia and diabetes mellitus (DM) are two of the most prevalent and disabling non-communicable diseases of old age, and their frequent co-occurrence has emerged as a major public health concern.1 Epidemiological evidence consistently demonstrates that type 2 DM is associated with an increased risk of both vascular dementia and Alzheimer's disease (AD), independent of shared risk factors such as hypertension, dyslipidaemia, and ApoE genotype.1 DM has also been identified as an independent predictor of post-stroke dementia, and the atherogenic burden of chronic hyperglycaemia is thought to potentiate cerebrovascular injury, thereby accelerating the clinical expression of underlying neurodegenerative pathology.1 The pathophysiological basis linking DM to cognitive decline is multifactorial. Chronic hyperglycaemia and hyperinsulinaemia promote the formation of advanced glycation end-products (AGEs) and reactive oxygen species, both implicated in the biological mechanisms of brain ageing and in the etiopathogenesis of AD.1,2 At the cellular level, competition between insulin and amyloid-beta for the insulin-degrading enzyme (IDE) may impair amyloid clearance in states of hyperinsulinaemia, while tau hyperphosphorylation, amyloid oligomerisation, and diffuse cerebral microangiopathy further contribute to structural brain injury in diabetic individuals.2 These mechanisms manifest radiologically as white matter hyperintensities, cortical and subcortical atrophy, and hippocampal volume loss, changes that correlate with impaired performance across memory, executive function, and processing speed domains.3,4

Magnetic Resonance Imaging (MRI) remains the most robust non-invasive modality for characterising these structural alterations in vivo. Conventional visual rating scales, however, are subject to inter-observer variability and lack the sensitivity required to detect subtle, region-specific volume changes. The advent of artificial intelligence (AI)-based automated MRI volumetry software has substantially improved the precision and reproducibility of quantitative brain

measurements, enabling objective assessment of parameters such as cerebral gray and white matter volume, cortical volume, and hippocampal volume.3,5 Recent functional and structural connectivity studies using such quantitative approaches have further reinforced that type 2 DM-related cognitive impairment is associated with measurable, localisable brain network and volumetric alterations rather than being a purely clinical diagnosis of exclusion.5,6

Despite this growing body of evidence, most existing studies have compared MRI findings between diabetic and non-diabetic individuals in the general population, or between diabetic patients with and without cognitive impairment.7 Comparatively few studies have examined brain volumetric differences specifically within a cohort of patients already diagnosed with dementia, stratified by DM status using rigorous, prospectively applied laboratory criteria. This distinction is clinically important: in patients presenting with an established dementia syndrome, it remains unclear whether comorbid DM independently contributes to a greater magnitude of regional brain volume loss, or whether age accounts for the observed differences.

Need for the Study

There is a clear gap in the literature regarding the independent contribution of DM to quantitative brain volume change specifically within a dementia population, as opposed to a diabetic population screened for cognitive impairment. Most prior work has also relied on manual or semi-automated volumetric techniques, which are time-intensive and prone to measurement variability, limiting their translational applicability in routine clinical settings.5 The use of AI-based automated MRI volumetry offers a reproducible, standardised, and clinically scalable method to quantify cerebral gray and white matter, cortical, and hippocampal volume loss, and is therefore well suited to answering this question with greater precision than has previously been possible.

An ambispective design — retrospectively identifying dementia patients and their imaging parameters from institutional records, while prospectively confirming DM status against ADA laboratory reference standards — allows this study to overcome the classification bias inherent in purely retrospective diabetes ascertainment, while still leveraging existing volumetric imaging data. Establishing whether DM is independently associated with brain volume change after adjusting for age would help clarify whether comorbid DM should be regarded as a factor relevant to structural brain injury in dementia, and would support the case for incorporating quantitative AI-based volumetry into the routine neuroimaging work-up of dementia patients with comorbid DM.

Aim

To determine whether diabetes mellitus (DM), confirmed prospectively by laboratory reference standards, is associated with quantitative brain volume change in patients with dementia, as measured by automated AI-based MRI volumetry.

Objectives

1. To retrospectively identify patients with a clinical diagnosis of dementia from institutional records and retrieve their AI-based brain volumetric parameters — global cerebral gray and white matter volume, cerebral cortex volume loss, and hippocampal volume (right and left).
2. To prospectively classify these patients as DM-positive or DM-negative based on laboratory reference standards (fasting plasma glucose and/or HbA1c, as per ADA criteria).
3. To compare AI-quantified brain volumetric parameters between DM-positive and DM-negative dementia patients.
4. To determine whether age independently influences brain volume, and whether the DM–volume association persists after adjusting for age.

MATERIALS AND METHODS

Study Design

An ambispective (retrospective–prospective) cohort study. The dementia cohort and their existing AI-based MRI volumetric reports were identified retrospectively from clinical records; diabetes status was then ascertained prospectively at follow-up using laboratory reference standards, rather than relying on retrospective chart-documented history, reducing misclassification of the exposure variable.

Study Population

One hundred (N = 100) patients with a clinical diagnosis of dementia, aged 34–88 years, who had an existing AI-based MRI dementia volumetry report on file, were included. Patients were subsequently classified as DM-positive (n = 64) or DM-negative (n = 36) based on laboratory criteria (HbA1c ≥ 6.5% and/or fasting plasma glucose ≥ 126 mg/dL, per ADA criteria).

Outcome Measures (AI-Based Volumetric Parameters)

- Global cerebral gray and white matter (GWM) volume loss (mm^3)

- Cerebral cortex (CC) volume loss (mm^2)
- Hippocampal atrophy measurement, right and left (HA Right, HA Left) (mm)

All parameters were derived from T1-weighted MRI processed through AI-based automated dementia-volumetry software, which quantifies regional brain parenchymal volume and expresses it against an age-matched normative population.

Statistical Analysis

- Descriptive statistics (mean ± SD, median, IQR, range, 95% CI) were computed for age and each volumetric parameter.
- Between-group comparisons (DM-positive vs DM-negative) were performed using the independent-samples t-test, with Welch's correction applied where Levene's test indicated unequal variances.
- Pearson correlation was used to assess associations between age and each volumetric parameter, and among the volumetric parameters themselves.
- Univariate ANCOVA (Type III sum of squares; volume ~ age + DM status) was used to determine whether DM–volume associations persisted after adjustment for age.
- Statistical significance was set at $p < 0.05$. All analyses were performed using IBM SPSS Statistics, Version 26.

RESULTS

Baseline Characteristics of the Study Population

A total of 100 subjects were included in the analysis. The mean age was 73.48 ± 10.54 years (range 34–88 years). Descriptive statistics for age and the neuroimaging parameters — global gray and white matter (GWM), cerebral cortex (CC), and hippocampal atrophy right and left (HA Right, HA Left) — are presented in Table 1.

Table 1. Descriptive Statistics of Age and Brain Volume Parameters (N = 100)

Variable	Mean ± SD	Median (IQR)	Range	95% CI for Mean
Age (years)	73.48 ± 10.54	76.0 (13.0)	34–88	71.39–75.57
GWM (mm^3)	774.49 ± 81.82	757.0 (105.0)	625–994	758.26–790.72
CC (mm^2)	428.34 ± 44.56	421.0 (66.0)	353–565	419.50–437.18
HA Right (mm)	2.61 ± 0.50	2.70 (0.70)	1.6–3.7	2.51–2.71
HA Left (mm)	2.45 ± 0.38	2.40 (0.40)	1.5–3.5	2.37–2.52

SD, standard deviation; IQR, interquartile range; CI, confidence interval; GWM, global gray and white matter; CC, cerebral cortex.

Shapiro-Wilk testing indicated that none of the study variables followed a normal distribution ($p < 0.05$ for all, except HA Right in the non-DM subgroup, $p = 0.080$). Age and GWM showed skewness of –1.824 and 0.564, respectively, consistent with the non-normal distribution confirmed by both the Kolmogorov–Smirnov and Shapiro–Wilk tests.

2 Prevalence of Diabetes Mellitus and Medication Use

Of the 100 subjects, 64 (64.0%) had a diagnosis of DM and 36 (36.0%) did not. Among all subjects, 48 (48.0%) were on DM medication and 52 (52.0%) were not.

Table 2. Association between DM Status and DM Medication Use

DM status	On medication, n (%)	Not on medication, n (%)	Total
No DM (n = 36)	0 (0.0%)	36 (100.0%)	36
DM (n = 64)	48 (75.0%)	16 (25.0%)	64
Total	48 (48.0%)	52 (52.0%)	100

Pearson $\chi 2 = 51.92$, df = 1, $p < 0.001$; Fisher's exact $p < 0.001$.

A strong, statistically significant association was observed between DM status and use of DM medication ($\chi^2 = 51.92$, df = 1, $p < 0.001$; Fisher's exact $p < 0.001$), confirming that medication use tracked closely with diagnosed DM status in this sample.

3 Comparison of Brain Volume Parameters between DM and Non-DM Groups

Independent-samples t-tests (with Welch correction applied where Levene's test indicated unequal variances) were used to compare age and neuroimaging parameters between subjects with and without DM. Results are summarised in Table 3.

Table 3. Comparison of Age and Brain Volume Parameters by DM Status

Variable	No DM (n=36) Mean ± SD	DM (n=64) Mean ± SD	t (df)	p-value
Age (years)	72.86 ± 8.29	73.83 ± 11.66	–0.48 (92.6)	0.631
GWM (mm^3)	747.94 ± 105.49	789.42 ± 60.89	–2.17 (48.4)	0.035*
CC (mm^2)	415.36 ± 57.31	435.64 ± 33.84	–1.94 (49.0)	0.058
HA Right (mm)	2.57 ± 0.60	2.63 ± 0.44	–0.52 (56.5)	0.606
HA Left (mm)	2.53 ± 0.50	2.40 ± 0.28	1.50 (47.9)	0.140

*p < 0.05. Welch (unequal-variance) t and df reported for GWM, CC, HA Right and HA Left, where Levene's test was significant (p < 0.05); equal-variance t reported for age (Levene p = 0.475).
Subjects with DM had a significantly higher mean GWM volume loss than those without DM (789.42 ± 60.89 vs 747.94 ± 105.49; t(48.4) = –2.17, p = 0.035; mean difference –41.48, 95% CI –80.0 to –3.0). CC was also higher in the DM group, approaching but not reaching conventional significance under the Welch correction (435.64 ± 33.84 vs 415.36 ± 57.31; t(49.0) = –1.94, p = 0.058); the equal-variance test for the same comparison was significant (t(98) = –2.23, p = 0.028; mean difference –20.28, 95% CI –38.34 to –2.22). Age, HA Right, and HA Left did not differ significantly between groups (p = 0.631, 0.606, and 0.140, respectively).

4 Correlation between Age and Brain Volume Parameters

Pearson correlation analyses were performed to examine relationships among age, GWM, CC, HA Right, and HA Left (Table 4). Age did not correlate significantly with any neuroimaging parameter. However, all neuroimaging parameters were significantly and positively inter-correlated, most strongly between GWM and CC (r = 0.867, p < 0.001).

Table 4. Pearson Correlation Coefficients between Study Variables (N = 100)

Variable	Age	GWM	CC	HA Right	HA Left
Age	1	–0.053	–0.161	–0.159	–0.161
GWM	–	1	0.867**	0.638**	0.522**
CC	–	–	1	0.647**	0.435**
HA Right	–	–	–	1	0.679**
HA Left	–	–	–	–	1

**Correlation significant at the 0.01 level (2-tailed). Age correlations with all four parameters were non-significant (p > 0.10).

5 Age-Adjusted Comparison of Brain Volume Parameters by DM Status

Because age is a known determinant of brain volume, univariate ANCOVA (Type III sum of squares) was used to compare each neuroimaging parameter between DM and non-DM groups after adjusting for age. Results are shown in Table 5.

Table 5. Age-Adjusted Comparison of Brain Volume Parameters by DM Status (ANCOVA)

Dependent variable	Effect	F	df	p-value	Adj. R^2
GWM	Age	0.42	1, 97	0.519	0.045
	DM status	6.33	1, 97	0.014*	
CC	Age	3.06	1, 97	0.083	0.058
	DM status	5.41	1, 97	0.022*	
HA Right	Age	2.62	1, 97	0.109	0.009
	DM status	0.41	1, 97	0.523	
HA Left	Age	2.43	1, 97	0.123	0.034
	DM status	2.82	1, 97	0.096	

*p < 0.05. Model: dependent variable ~ Age (covariate) + DM status.
After adjusting for age, DM status remained a significant independent predictor of both GWM (F(1,97) = 6.33, p = 0.014) and CC (F(1,97) = 5.41, p = 0.022), while age itself was not a significant covariate for either parameter (p = 0.519 and p = 0.083, respectively). DM status was not significantly associated with HA Right (p = 0.523) or HA Left (p = 0.096) after age adjustment, although the trend for HA Left approached significance.

6 Summary of Key Findings

DM was present in 64% of the study population and was strongly associated with DM medication use (p < 0.001). Subjects with DM showed significantly higher GWM volume loss than those without DM, both in unadjusted (p = 0.035) and age-adjusted (p = 0.014) analyses, and higher CC volume loss values that reached significance in the equal-variance unadjusted comparison (p = 0.028) and the age-adjusted analysis (p = 0.022). Hippocampal atrophy measurements (HA Right, HA Left) did not differ significantly by DM status in either unadjusted or age-adjusted analyses. Age was not significantly correlated with any neuroimaging parameter, whereas GWM, CC, HA Right, and HA Left were all significantly and positively inter-correlated (p < 0.001 for all pairs).

DISCUSSION

1 Overview of Principal Findings

This study examined the association between diabetes mellitus (DM) and quantitative, AI-derived MRI volumetric parameters — global gray and white matter (GWM), cerebral cortex (CC), and right and left hippocampal measurements — among 100 subjects with a mean age of 73.48 ± 10.54 years, of whom 64% had DM. DM was significantly associated with higher GWM and CC measurements, an association that persisted after adjustment for age, while no significant

association was found for either hippocampal measurement. These findings are discussed below in relation to the existing literature on diabetes-related brain structural change.[1,2,3,4,5,6,7]

2 Diabetes Mellitus and White Matter: Reconciling an Unexpected Direction

The literature on DM and cerebral white matter is extensive and fairly consistent in direction: chronic hyperglycaemia and hyperinsulinaemia are held to accelerate white-matter injury through advanced glycation end-products (AGEs), oxidative stress, and diffuse cerebral microangiopathy, manifesting as white matter hyperintensities (WMH) on MRI.[1,2] Gavali et al. directly demonstrated this pattern in a comparative MRI study of type 2 diabetics with and without cognitive impairment, reporting significantly higher Fazekas WMH scores and lower hippocampal volume in the cognitively impaired diabetic group, with WMH burden correlating negatively with MoCA performance ($r = -0.56$).[7] Similarly, reviews of structural and functional connectivity in diabetes-related cognitive impairment describe white matter tract disruption and reduced structural integrity on diffusion tensor imaging as a hallmark finding.[3,5]

The present study's finding of a higher mean GWM volume loss in the DM group (789.42 ± 60.89 mm³) compared with the non-DM group (747.94 ± 105.49 mm³), significant even after age adjustment ($F(1,97) = 6.33$, $p = 0.014$), therefore runs counter to the general direction reported in this body of literature. Several explanations may account for this divergence and merit discussion rather than being dismissed as anomalous:

• WMH misclassification within "global gray and white matter." AI-based volumetric software typically quantifies total white-matter tissue-class volume rather than lesion load specifically. If hyperintense diabetic white-matter lesions were segmented as part of the white-matter compartment rather than as a separate WMH mask, an increased lesion burden could paradoxically inflate the measured GWM volume loss rather than reduce it — the opposite of what is captured by lesion-specific scoring systems such as Fazekas grading.

• Population and disease-stage differences. The present cohort consisted exclusively of patients with an established dementia diagnosis, whereas most comparator literature examined diabetic patients drawn from general or diabetology populations, stratified secondarily by cognitive status. In patients who already have dementia, the relationship between DM and white-matter measurement may be shaped more strongly by neurodegenerative and compensatory processes than by the vascular mechanisms that dominate in non-demented diabetic cohorts.

• Unmeasured DM-related covariates. Diabetes duration, glycaemic control (HbA1c), and vascular comorbidities were not available for adjustment in the present analysis, limiting direct comparability with studies in which such variables were the principal drivers of observed white-matter differences.

Taken together, the association identified here should be interpreted as evidence that DM status is statistically linked to GWM measurement in this dementia cohort, not as evidence that DM preserves or increases white-matter volume in a biologically protective sense, nor as a replication of the atrophic/WMH pattern described in the literature.[7]

3 Diabetes Mellitus and Cerebral Cortex Volume

Findings for cerebral cortex (CC) volume loss followed a pattern concordant with GWM, with a higher mean CC measurement in the DM group (435.64 ± 33.84 mm² vs 415.36 ± 57.31 mm²) that was significant on the equal-variance comparison ($p = 0.028$) and became clearly significant after age adjustment ($F(1,97) = 5.41$, $p = 0.022$). Cortical thickness and cortical volume are among the most frequently examined structural correlates of diabetes-related cognitive impairment. Gavali et al. reported a significantly thinner cortex in cognitively impaired diabetics compared with unimpaired diabetics (2.38 ± 0.12 vs 2.46 ± 0.11 mm; $p < 0.001$), consistent with a pattern of cortical thinning driven by chronic hyperglycaemia.[7] Reviews of diabetes-related brain change similarly describe cortical and subcortical atrophy as a core structural feature, and regional gray-matter analyses have identified diabetes-associated volume loss extending across cortical regions.[1,4]

The direction of the present finding — higher, rather than lower, CC volume loss in the DM group — diverges from this atrophic pattern and, as with GWM, is unlikely to reflect a genuinely protective effect of DM on cortical structure. The most plausible explanations mirror those discussed for GWM: differences in segmentation methodology between volumetric software and lesion/thickness-based scoring systems, the dementia-selected nature of this cohort (in which cortical change may already be advanced and less discriminative between DM and non-DM patients than in pre-dementia diabetic populations), and the absence of adjustment for diabetes duration, glycaemic control, and vascular risk factors, each of which independently predicted MRI change in comparable cohorts.[7] The strong positive correlation between GWM and CC observed in this study ($r = 0.867$, $p < 0.001$, Section 5.5) further suggests that both parameters are capturing a shared, overlapping structural signal rather than two fully independent measurements, which may partly explain why both showed a concordant direction of association with DM.

4 Diabetes Mellitus and Hippocampal Volume: A Contrast with Prior Literature

In contrast to GWM and CC, neither right nor left hippocampal measurement differed significantly by DM status in this study ($p = 0.606$ and $p = 0.140$, respectively; age-adjusted $p = 0.523$ and $p = 0.096$). This is a notable departure from a substantial portion of the literature, in which hippocampal atrophy is one of the most consistently reported structural

correlates of diabetes-related cognitive impairment. Gavali et al. found significantly lower hippocampal volume in cognitively impaired diabetics (6.2 ± 0.7 cm^3) compared with unimpaired diabetics (6.8 ± 0.6 cm^3, $p < 0.001$), with hippocampal volume positively correlated with MoCA score ($r = +0.49$).[7] Roy et al., using regional gray-matter analysis, similarly identified diabetes-associated regional atrophy encompassing medial temporal structures.[4] Mechanistically, this is attributed to hyperinsulinaemia-driven competition for the insulin-degrading enzyme, impairing amyloid-beta clearance in hippocampal and medial temporal regions, alongside tau hyperphosphorylation and amyloid oligomerisation.[2]

Given that the present cohort already carried a dementia diagnosis, one plausible interpretation is a ceiling/floor effect: hippocampal atrophy may already be advanced and relatively uniform across both DM and non-DM patients once dementia is established, such that DM status no longer discriminates hippocampal volume at this later disease stage, even though it may be a more powerful discriminator earlier in the disease course, as suggested by studies conducted in pre-dementia diabetic cohorts.[7] This would be consistent with the broader concept that DM-related and neurodegenerative pathological cascades converge onto a common final atrophic pathway once dementia is clinically manifest, a possibility raised in earlier reviews of the DM–dementia relationship.[1] The p-value of 0.096 for the age-adjusted left hippocampal comparison is worth noting as a trend that approached, but did not reach, conventional significance, and may reflect inadequate power in this sample of 100 rather than a true absence of effect.

5 Correlation Between Age and Neuroimaging Parameters

Unlike DM status, age was not significantly correlated with any of the four volumetric parameters (GWM $r = -0.053$, CC $r = -0.161$, right hippocampus $r = -0.159$, left hippocampus $r = -0.161$), and adjustment for age did not attenuate the DM associations with GWM or CC — if anything, adjustment strengthened the CC association from a borderline unadjusted result to a clearly significant one. This pattern differs from much of the diabetes-neuroimaging literature, in which age is typically a strong independent predictor of atrophy and is carefully modelled as a confounder alongside diabetes duration and HbA1c.[7] The absence of an age effect in this cohort may reflect the restricted, older, and dementia-selected nature of the sample, in which age-related variance in brain volume may already be compressed at the upper end of the age distribution (range 34–88 years, mean 73.48 years).

The strong positive inter-correlations among the neuroimaging parameters themselves — particularly between GWM and CC ($r = 0.867$, $p < 0.001$) — are consistent with the expected anatomical and physiological relationship between global white-matter integrity and cortical structure, and lend internal coherence to the parameter-specific pattern of DM association reported here.[3,5]

6 Overall Interpretation and Clinical Implications

Considered against the wider literature, this study both aligns with and diverges from prior findings in informative ways. It aligns with the well-established observation that DM has a measurable, region-specific rather than diffuse relationship with brain structure, a theme running through both mechanistic reviews[1,2] and imaging-based comparative studies.[3,4,7] It diverges from the literature in the direction of the GWM and CC findings and in showing no discriminative hippocampal effect, and both divergences are most plausibly explained by methodological factors (segmentation of WMH within total white-matter volume) and by cohort selection (a dementia-only population, in contrast to diabetic populations stratified by cognitive status), rather than by a genuinely protective effect of DM on brain structure.

Clinically, these findings reinforce two points consistent with the literature: first, that automated AI-based volumetry is sensitive enough to detect DM-related structural differences even within a moderate-sized, single-diagnosis cohort, supporting its incorporation into dementia work-up as suggested elsewhere;[3,5] and second, that any observed DM–volume association in such analyses requires careful interpretation against segmentation methodology, disease stage, and unmeasured metabolic covariates (duration of DM, HbA1c, vascular risk factors) before being assigned biological meaning, a caution echoed in the primary literature on this topic.[1,7]

7 Limitations

Compared with the more detailed diabetic-cognitive-impairment literature reviewed here, the present study did not capture diabetes duration, glycaemic control, or vascular risk factors, all of which were shown to be independent predictors of MRI change in comparable cohorts.[7] It also did not employ lesion-specific WMH scoring (e.g., Fazekas grading) alongside volumetric segmentation, which may account for the counterintuitive direction of the white-matter and cortical findings relative to prior work.[7] Finally, the ambispective, single-centre, dementia-only design limits generalisability to diabetic populations without established dementia, where the DM–hippocampal relationship appears more pronounced in the literature.[7]

8 Summary

In summary, DM was significantly associated with higher GWM and CC measurements in this cohort, both before and after age adjustment, but showed no significant association with hippocampal volume. While region-specific DM–brain associations are well supported by the literature,[1,2,3,4,5,7] the direction of the GWM and CC findings and the absence of a hippocampal effect diverge from prior reports and are best explained by segmentation methodology and the dementia-selected nature of this cohort rather than by a protective biological effect of diabetes. Further studies incorporating diabetes duration, glycaemic control, and lesion-specific white-matter scoring, ideally in larger and longitudinally followed cohorts, are needed to clarify these relationships.

CONCLUSION

This study provides evidence of a significant association between diabetes mellitus and quantitative brain volumetric changes in patients with dementia, with the observed effects being region-specific rather than generalized across all brain structures. DM-positive patients demonstrated significantly higher global gray and white matter and cerebral cortex volume loss compared with DM-negative patients, and these associations remained significant after adjustment for age. In contrast, no significant association was observed between DM status and right or left hippocampal volume.

The significant positive inter-correlations among GWM, cerebral cortex, and bilateral hippocampal volume loss further indicate that AI-derived volumetric measures capture coordinated structural characteristics across different brain regions. Overall, the findings support diabetes mellitus as a metabolic factor associated with structural brain differences in dementia, particularly involving global white matter and cerebral cortex regions, though the direction of these associations warrants further clarification with lesion-specific imaging and adjustment for diabetes duration and glycaemic control. These results also highlight the potential utility of AI-based automated MRI volumetry for objectively identifying and quantifying diabetes-associated structural brain changes in patients with dementia.

Conflict of interest: Nil

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