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MRI-based correlations of mesial temporal atrophy, hippocampal volumetry, and inferior lateral ventricle–hippocampus ratio in Alzheimer's dementia

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Abstract

Background

Alzheimer's dementia (AD) is characterized by medial temporal lobe atrophy, particularly involving the hippocampus, and secondary enlargement of the inferior lateral ventricles. The Mesial Temporal Atrophy (MTA) visual scale is widely used in clinical practice but is inherently subjective, while quantitative MRI-based measurements may provide greater objectivity.

Objective

To evaluate the correlation between the MTA visual scale, hippocampal volumetry, and the inferior lateral ventricle–hippocampus (ILV/HPC) ratio in patients with Alzheimer's dementia.

Methods

This ambispective study included thirty-six patients with Alzheimer's dementia who underwent brain MRI between January 2022 and July 2025. Visual MTA scoring and automated volumetric measurements of the hippocampus and inferior lateral ventricle were performed. Inter-reader reliability and correlations between imaging parameters were statistically analyzed.

Results

Thirty-six patients were included. Inter-reader agreement for MTA scoring was almost perfect (Cohen's κ = 0.851–0.889). The MTA score showed a moderate negative correlation with hippocampal volume ($r = -0.341$; $p = 0.042$) and a very strong positive correlation with the ILV/HPC ratio ($r = +0.843$; $p < 0.001$). Multivariate analysis demonstrated that hippocampal and inferior lateral ventricle volumes were independent predictors of MTA score ($R^2 = 0.616$).

Conclusion

There is a significant correlation between the MTA visual scale, hippocampal volumetry, and the inferior lateral ventricle–hippocampus ratio. The inferior lateral ventricle–hippocampus ratio demonstrated the strongest correlation with the MTA score and may serve as a simple quantitative biomarker for assessing medial temporal atrophy in Alzheimer's dementia.

Background

Alzheimer's disease is the leading cause of dementia in older adults, characterized by progressive neurodegeneration and neuronal loss. Early and accurate diagnosis is essential, as timely intervention can improve clinical outcomes in a brain with limited regenerative capacity. Structural MRI provides key biomarkers for AD, particularly in the medial temporal lobe.[1–3]

Medial temporal lobe atrophy, especially hippocampal atrophy, is a hallmark imaging feature and correlates with cognitive decline. Hippocampal volumetry is a well-established quantitative method to measure atrophy but is time-consuming, requires specialized software, and is influenced by individual anatomical variability, such as cranial size. The MTA visual scale offers a simple, semi-quantitative alternative with good diagnostic performance; however, it remains subjective and may be less sensitive in early disease stages[4, 5].

In addition to hippocampal atrophy, enlargement of the inferior lateral ventricle reflects secondary ex-vacuo dilatation due to adjacent hippocampal loss. The ILV/HPC ratio, which combines hippocampal volume and ventricular size, has been proposed as a complementary biomarker. This ratio may offer several advantages over hippocampal volume alone. By considering ventricular size relative to hippocampal volume, it accounts for differences in cranial size and individual anatomical variation. Moreover, early neurodegenerative changes may lead to noticeable ventricular expansion before absolute hippocampal volume loss becomes pronounced, enhancing sensitivity to subtle atrophy. Finally, using a ratio improves reproducibility by reducing the influence of absolute volumetric measurement errors, potentially minimizing inter-rater variability [6–9].

Therefore, this study aimed to evaluate the correlation between the MTA visual scale, hippocampal volumetry, and the ILV/HPC ratio in patients with Alzheimer's disease. We hypothesize that MTA visual scores correlate with both hippocampal volume and ILV/HPC ratio, and that the ILV/HPC ratio may provide a more robust and objective measure of medial temporal atrophy than hippocampal volume alone.

Subjects and Methods

Study Design

This ambispective study combined retrospective and prospective data of Alzheimer's disease patients who underwent brain MRI with a 3D T1-weighted Turbo Field Echo (TFE) sequence using 1.5 T and 3 T MRI (Philips Achieva). To minimize scanner-related variability, all volumetric measurements were processed using the same automated pipeline and normalized to intracranial volume. Specifically, 20 patients were identified retrospectively from medical records between January 2022 – October 2024, while 16 patients were enrolled prospectively from November 2024 to July 2025. The study was approved by the Ethics Committee of the Faculty of Medicine, Pelita Harapan University (Approval No. 219/K-LKJ/ETIK/VI/2025). All methods were performed in accordance with the relevant guidelines and regulations.f

Patients were included if they had been clinically diagnosed with Alzheimer's dementia by a board-certified neurologist based on clinical evaluation and standardized cognitive or memory testing. As supportive diagnostic evidence, a subset of patients (n = 12) also underwent amyloid positron emission tomography imaging demonstrating amyloid positivity consistent with Alzheimer's disease pathology.

Eligible participants were required to have complete MRI data suitable for MTA assessment and volumetric analysis. Patients were excluded if they had a diagnosis of vascular dementia or a history or imaging evidence of cerebral infarction involving subcortical structures, the perihippocampal region, or the medial temporal lobe. Additional exclusion criteria included a history of intracranial tumors, prior brain surgery, or the presence of cerebral microbleeds detected on susceptibility-weighted imaging. Patients with incomplete medical records or insufficient imaging data were also excluded from the analysis.

MTA Visual Scale Assessment

The MTA visual score was assessed on coronal T1-3D TFE images aligned parallel to the brainstem at the level of the anterior pons. Two board-certified radiologists (with 30 and 22 years of experience in neuroradiology and one senior radiology resident (with 4 years of training) independently rated each case. In case of discrepancy, the senior radiologist determined the final score. All raters were blinded to the clinical data and final diagnosis.

Volumetric Measurement

Hippocampal and inferior lateral ventricle volumetric data were obtained from T1-3D TFE images processed using VolBrain software. Absolute volumes were segmented automatically and normalized to intracranial volume (ICV), yielding relative hippocampal and inferior lateral ventricle fractions (% of ICV). The ILV/HPC ratio was calculated by dividing the inferior lateral ventricle volume by the hippocampal volume, with both volumes normalized to intracranial volume (%ICV).

Automated volumetric segmentation of the hippocampus and inferior lateral ventricle was performed using VolBrain software, which has been previously validated against expert manual segmentation. To ensure segmentation quality, all volumetric outputs were visually inspected for gross segmentation errors, including mislabeling or incomplete delineation of structures. Cases with inadequate segmentation quality or significant technical artifacts were excluded from the final analysis.

Statistical Analysis

Statistical analyses were performed using SPSS 26.0. Inter-reader reliability was evaluated with Cohen's κ. Correlations between variables were analyzed using Spearman's ρ. Variables with $p \leq 0.25$ in bivariate analysis were included in multivariate linear regression models. A p-value < 0.05 was considered statistically significant. Data distribution was assessed using the Shapiro–Wilk test. As several variables showed non-normal distribution, non-parametric statistical methods were applied. Outliers were evaluated visually using boxplots and were retained in the analysis unless attributable to clear technical or segmentation errors, which were excluded during quality control.

Results

Study Population

A total of 36 patients met the inclusion criteria (19 females [52.8%], 17 males [47.2%]). The majority were aged 75–84 years (41.7%), consistent with the typical demographic profile of Alzheimer's disease (Table 1).

Inter-reader reliability

Cohen's κ values indicated almost perfect agreement between all rater pairs: Reader 1 vs 2 = 0.852, Reader 2 vs 3 = 0.889, and Reader 1 vs 3 = 0.851 ($p < 0.001$ for all), according to Landis and Koch (1977).

Correlation analyses

• MTA vs Hippocampal Volume:

Moderate negative correlation ($r = -0.341$; 95% CI: −0.58 to − 0.02; $p = 0.042$) which means increasing MTA score was associated with decreasing hippocampal volume (Fig. 1).

• MTA vs ILV/HPC Ratio:

Very strong positive correlation ($r = +0.843$; 95% CI: 0.70 to 0.92; $p < 0.001$), indicating that higher MTA scores correspond to greater relative enlargement of the ILV compared to hippocampal volume (Fig. 2).

Multivariate analysis

Multiple linear regression identified hippocampal volume ($B = -0.289$; 95% CI: −0.55 to − 0.03; $p = 0.032$) and ILV volume ($B = 0.586$; 95% CI: 0.34 to 0.83; $p < 0.001$) as independent predictors of MTA visual score. The model explained 61.6% of the variance ($R^2 = 0.616$).

MTA Score = 2.026 − 0.289(Hippocampal Volume) + 0.586(ILV Volume)

Discussion

This study evaluated the relationship between MTA grading and quantitative MRI-derived parameters, namely hippocampal volume and the inferior lateral ventricle–hippocampus ILV/HPC ratio, in patients with Alzheimer's dementia. The results demonstrated a moderate inverse negative correlation between MTA scores and hippocampal volume, a very strong positive correlation scores between MTA scores and the ILV/HPC ratio, and excellent inter-rater reliability of visual MTA assessment.

In terms of demographic characteristics, females slightly predominated (52.8%). This finding is consistent with previous studies reporting a higher prevalence and faster pathological progression of

Alzheimer's dementia in women, which has been attributed to hormonal, genetic, and neuropathological factors, including a greater burden of neurofibrillary tau pathology and faster tau accumulation compared with men [10–13]. Beside that, postmortem neuropathological studies have shown higher NFT density in females even when amyloid load or overall atrophy levels are comparable to males[12, 13].

The most common age group in this study was 75–84 years, aligning with epidemiological data showing a sharp increase in Alzheimer's incidence in this age range [14, 15]. The relatively small proportion of patients aged ≥ 85 years reflects common recruitment challenges in advanced age groups, as reported in prior studies [16].

Inter-reader reliability analysis demonstrated almost perfect agreement, with Cohen's κ values ranging from 0.85 to 0.89. These results are comparable to those reported by Molinder et al[19] and exceed agreement levels described in earlier studies[17, 18]. The high consistency observed despite differing levels of reader experience supports the robustness and reproducibility of standardized MTA visual assessment in clinical practice. This emphasizes that the standardized MTA visual rating method can minimize variability across different levels of expertise, consistent with Hakansson et al[20].

The moderate inverse association between MTA score and hippocampal volume ($r = -0.341$; 95% CI: −0.58 to − 0.02; $p = 0.042$) indicates that higher MTA grades reflect reduced hippocampal size but are not solely determined by hippocampal volume. This is consistent with previous studies showing that the MTA scale captures a composite of medial temporal changes, including hippocampal shrinkage and enlargement of adjacent cerebrospinal fluid spaces such as the choroid fissure and inferior lateral ventricle [7, 23, 24]. Consequently, MTA grading and hippocampal volumetry should be regarded as complementary rather than interchangeable markers.

In contrast, the ILV/HPC ratio demonstrated a very strong positive correlation with MTA scores ($r = +0.843$; 95% CI: 0.70 to 0.92; $p < 0.001$), suggesting that this ratio closely reflects the visual components assessed in MTA grading. This finding is in line with Wittens et al. [7], Nestor et al. [27], and Rusinek et al. [28], who reported that inferior lateral ventricular enlargement is tightly linked to hippocampal atrophy and disease progression in Alzheimer's dementia. By incorporating both ventricular expansion and hippocampal loss, the ILV/HPC ratio appears to provide a more balanced and dynamic representation of medial temporal structural change than absolute hippocampal volume alone.

Multivariate regression analysis further supported this interpretation, identifying hippocampal volume and inferior lateral ventricle volume as independent predictors of MTA score, together explaining approximately 61.6% of its variance. These results indicate that visual MTA grading predominantly reflects true neurodegenerative changes rather than age-related volume variation, reinforcing its biological validity.

From a clinical perspective, these findings support the continued use of the MTA visual scale as a rapid and reliable screening tool in routine practice, particularly in settings where advanced post-processing is

not readily available. The strong correlation between MTA scores and the ILV/HPC ratio suggests that this ratio may serve as a simple quantitative adjunct, offering greater objectivity while remaining feasible for clinical implementation. Such an approach may be especially useful for longitudinal follow-up and research applications.

Technical Considerations

Magnetic field strength differences between 1.5 T and 3 T MRI scanners may introduce bias in volumetric or visual MTA analyses. The 3 T MRI provides a higher signal-to-noise ratio and better anatomical delineation than 1.5 T, making automatic segmentation and visual scoring potentially more sensitive[21]. To minimize discrepancies, this study employed a standardized T1-3D TFE isotropic acquisition protocol across both scanners. Furthermore, VolBrain software integrated the international Neuroimaging Consortium for the Evaluation of Alzheimer's (NICE) protocol and adhered to the EADC–ADNI Harmonized Protocol (HarP) for hippocampal segmentation, improving inter-scanner consistency. VolBrain also provides high reproducibility with shorter processing time, making it a reliable primary quantification tool[22, 23].

MRI field strength (1.5 T vs 3 T) can introduce bias in volumetric estimation due to differing signal-to-noise ratios and spatial resolution. This study minimized variability using standardized T1-3D TFE isotropic sequences and VolBrain's harmonized processing pipeline (EADC-ADNI HarP protocol, ensuring inter-scanner consistency.

Limitations

This study has several limitations. First, it was a single-center ambispective study with a modest sample size and an unequal distribution of MRI field strengths, with 1.5 T scanners used in 13 patients and 3 T scanners in 23 patients, which may limit generalizability and introduce potential scanner-related bias. Although standardized acquisition protocols and intracranial volume normalization were applied to mitigate variability, residual effects related to field strength differences cannot be fully excluded. Second, the cross-sectional design precludes assessment of longitudinal changes in medial temporal atrophy and disease progression. Future multicenter studies with larger cohorts, uniform scanner strength, and longitudinal follow-up are warranted to validate the ILV/HPC ratio as a biomarker of disease progression and clinical outcomes.

Future Research

Future multicenter studies with larger, more diverse cohorts, uniform imaging protocols, and longitudinal follow-up are warranted to validate the ILV/HPC ratio as a biomarker of disease progression and clinical outcomes.

Conclusion

The present study demonstrated a moderate negative correlation between the Mesial Temporal Atrophy (MTA) visual scale and hippocampal volume, indicating that higher MTA scores are associated with smaller hippocampal volumes. In contrast, a very strong positive correlation was observed between MTA scores and the inferior lateral ventricle–hippocampus (ILV/HPC) ratio, suggesting that increasing medial temporal atrophy is accompanied by a disproportionate enlargement of the inferior lateral ventricle relative to hippocampal size. Multivariate analysis further confirmed that hippocampal volume and inferior lateral ventricle volume were independent predictors of the MTA visual score, together accounting for 61.6% of its variance. Overall, these findings suggest that the ILV/HPC ratio shows promise as a quantitative complement to visual MTA assessment for evaluating medial temporal atrophy in Alzheimer's disease. However, larger studies with independent cohorts are warranted to further validate its clinical utility and generalizability.

Abbreviations

ADNI
Alzheimer's Disease Neuroimaging Initiative
EADC
European Alzheimer's Disease Consortium
HPC
Hippocampus
ICV
Intracranial Volume
ILV
Inferior Lateral Ventricle
MRI
Magnetic Resonance Imaging
MTA
Mesial Temporal Atrophy
NFT
Neurofibrillary Tau
NICE
Neuroimaging Consortium for the Evaluation of Alzheimer's
TFE
Turbo filed echo
T1
WI-T1 Weighted Image

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Faculty of Medicine, Pelita Harapan University (Approval No. 219/K-LKJ/ETIK/VI/2025). All methods were performed in accordance with the relevant guidelines and regulations.

Written informed consent was obtained from all participants or their legally authorized representatives for the prospective component of the study. For the retrospective component, the requirement for informed consent was waived by the Ethics Committee due to the use of fully anonymized data.

Consent for publication

Not applicable.

Competing interest

The authors declare no competing interests.

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Author Contribution

Debora Semeia Takaliuang: Conceptualization, Methodology, Software, Data curation, Writing- Original draft preparation. Rusli Muljadi, Ratna Sutanto: Visualization, Investigation. Rocksy Fransisca: Supervision. Debora Semeia Takaliuang, Rusli Muljadi: Software, Validation. Ratna Sutanto, Debora Semeia Takaliuang, Cucunawangsih: Writing- Reviewing and Editing

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Tables

Table 1
Sample characteristic

Characteristic	Mean ± SD (Min–Max)	n (%)
Age (years)		—
< 65 years	—	7 (19%)
65–74 years	—	13 (36%)
75–84 years	—	15 (42%)
> 85 years	—	1 (3%)
Sex distribution		
Female	—	19 (53%)
Male	—	17 (47%)
Scanner type		
1.5 T Phillips		13 (36%)
3 T Phillips		23 (64%)
MTA Visual Score	1.91 ± 0.2 (0–4)	—
ILV Volume	2.71 ± 0.24 (0.68–6.67)	—
Hippocampal Volume	5.87 ± 0.17 (0.35–7.83)	—
ILV/HPC Ratio	0.47 ± 0.49 (0.11–1.43)	—

Figures

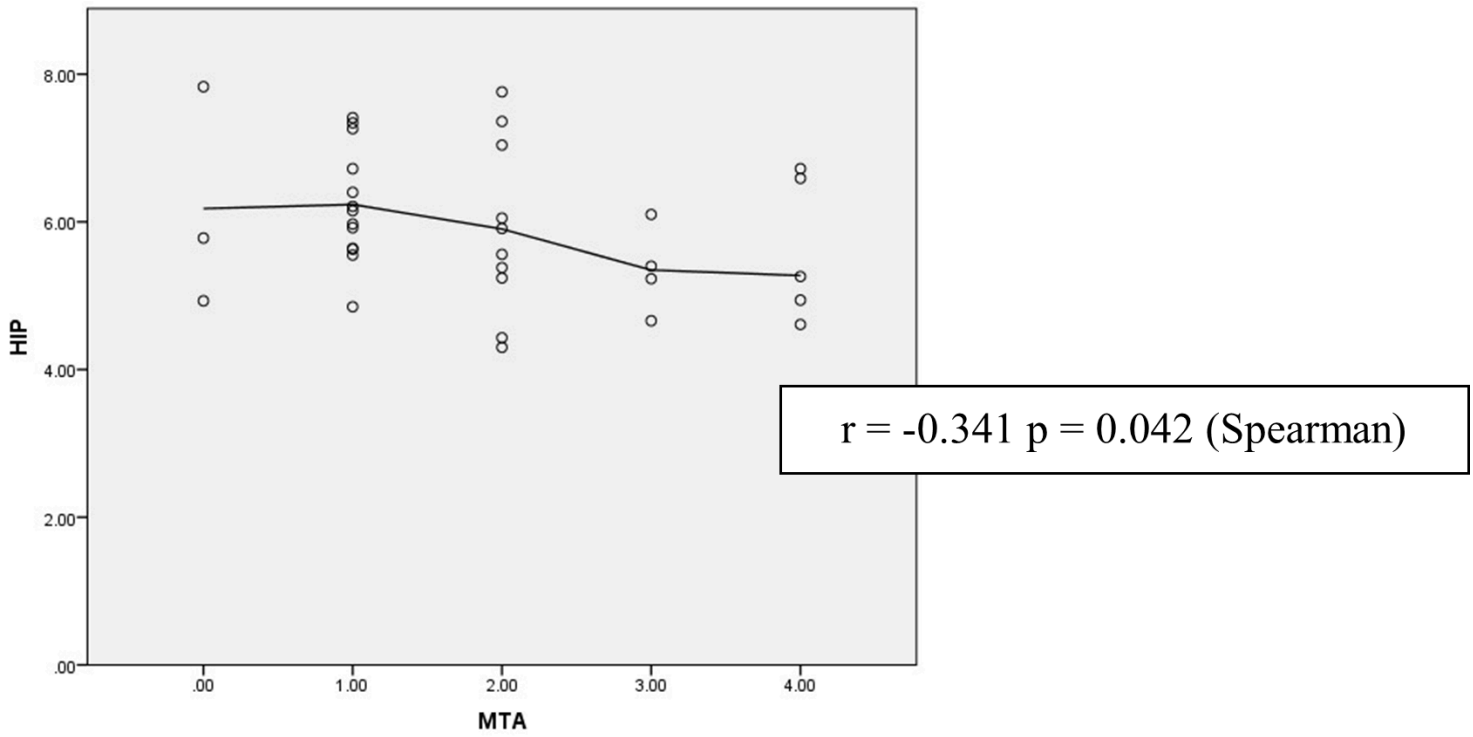


Figure 1

Scatter plot showing the correlation between the visual MTA scale and hippocampal volumetry. Each circular dot represents an individual subject (patient) with corresponding values of the visual MTA scale and hippocampal volume. The curved line in the middle indicates the local regression line, illustrating the general relationship pattern between the visual MTA scale and hippocampal volumetry, demonstrating a trend of decreasing hippocampal volume with increasing visual MTA scale scores.

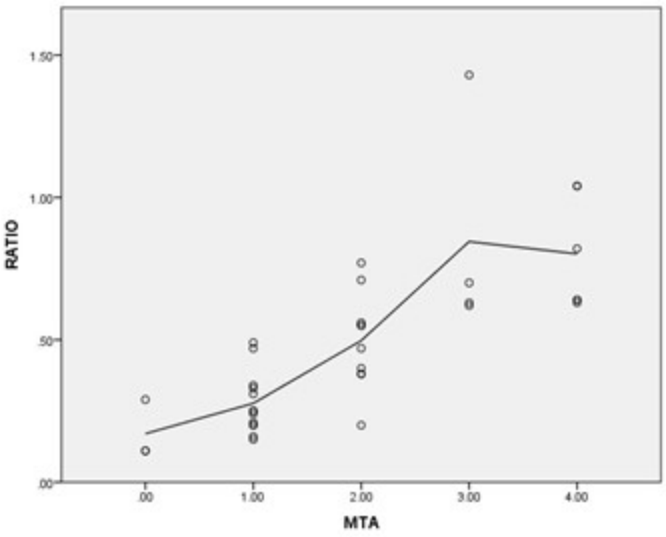


Figure 2

Scatter plot showing the correlation between the visual MTA scale and the inferior lateral ventricle–hippocampus ratio.Each circular dot represents an individual subject (patient) with corresponding values

of the visual MTA scale and the inferior lateral ventricle–hippocampus ratio. The curved line in the middle illustrates a positive relationship between the MTA scale and the inferior lateral ventricle–hippocampus ratio, indicating that hippocampal atrophy is associated with a relative enlargement of the inferior lateral ventricle.