

AI-Based Grading of Brain Atrophy in Alzheimer's Disease: A Comparison against the Scheltens' Visual Rating Scale

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01 Background & Objective

- Medial temporal lobe (MTL) atrophy is among the earliest and most robust MRI markers of Alzheimer's disease (AD) — a core neurodegeneration (N) biomarker in the NIA-AA AT(N) framework.
- The **Scheltens visual MTA scale (0–4)** is the most widely used grading method, but it is **subjective, ordinal/coarse, age-dependent, and prone to inter-rater variability**, with limited sensitivity to early change.
- The **occupancy index** captures, in a single ratio, both hippocampal volume loss **and** compensatory inferior lateral ventricle (ILV) expansion — tracking the atrophic process more faithfully than volume alone.

OBJECTIVES

Develop an **AI-based atrophy-grading** approach using automated volumetric **occupancy indices**, and benchmark it against conventional visual MTA scoring for discriminating cognitively normal (CN) from AD participants.

02 Methods

Participants (Table 1)

- 300 ADNI participants: **150 CN** and **150 AD**, aged **55–89 yr**.
- Balanced for **age and sex** (sex $p = 0.817$; age-group $p = 0.719$; mean age 73.1 vs 73.0 yr).
- CN: MMSE ≥ 24 , CDR 0. AD: NIA-AA criteria for probable AD dementia.

AI segmentation (Figure 1)

- 3D **T1-weighted MRI** processed with **Neurophet AQUA** (deep-learning Split-Attention U-Net) for automated whole-brain segmentation and regional volumes.
- AQUA validated across MRI field strengths, multi-center settings, and ethnically diverse cohorts.

Occupancy indices

$$\text{Occupancy index}_{\text{Target region}} = \frac{\text{Volume}_{\text{Target region}}}{\text{Volume}_{\text{Target region}} + \text{Volume}_{\text{Inferior lateral ventricle}}}$$

- HOC** = Hippocampal volume $\div$ (Hippocampal volume + ILV volume)
- mTOC** = Medial temporal cortex volume $\div$ (Medial temporal cortex volume + ILV volume)
- min-HOC / min-mTOC** = value of the more-atrophied hemisphere (per-hemisphere minimum).
- Index range 0–1; **lower = greater atrophy**.

Visual reference standard

- Scheltens MTA rated on **coronal T1** by **two board-certified neuroradiologists**, blinded to diagnosis; disagreements resolved by consensus.
- Max MTA** = higher of the left/right hemispheric scores.

Table 1. Age and sex distribution (CN vs AD)

	CN (N=150)	AD (N=150)	p-value
Sex			0.817
Female	78 (52.0%)	75 (50.0%)	
Male	72 (48.0%)	75 (50.0%)	
Age group			0.719
50s	9 (6.0%)	14 (9.3%)	
60s	51 (34.0%)	46 (30.7%)	
70s	46 (30.7%)	46 (30.7%)	
80s	44 (29.3%)	44 (29.3%)	

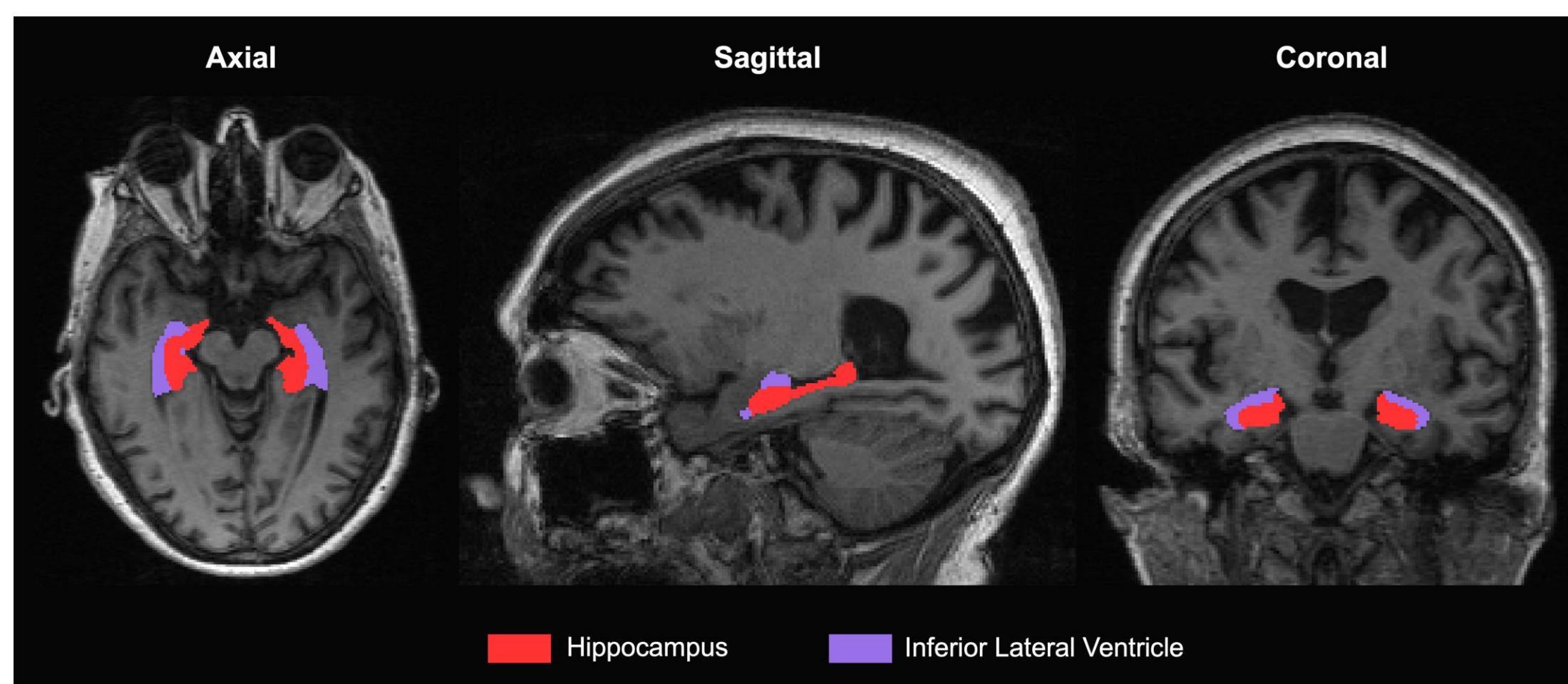


Figure 1. AQUA segmentation of the hippocampus (red) and inferior lateral ventricle (purple). The occupancy index is the ratio of regional volume to (regional volume + ILV volume).

Statistical analysis

- Group differences (HOC, mTOC, min-HOC, min-mTOC, Max MTA): independent two-sample t-tests.
- AD classification: **support vector machine (SVM)** classifiers on occupancy-index features (HOC, mTOC, min-HOC, min-mTOC), compared with a **Max MTA** model. Performance = AUC and accuracy.

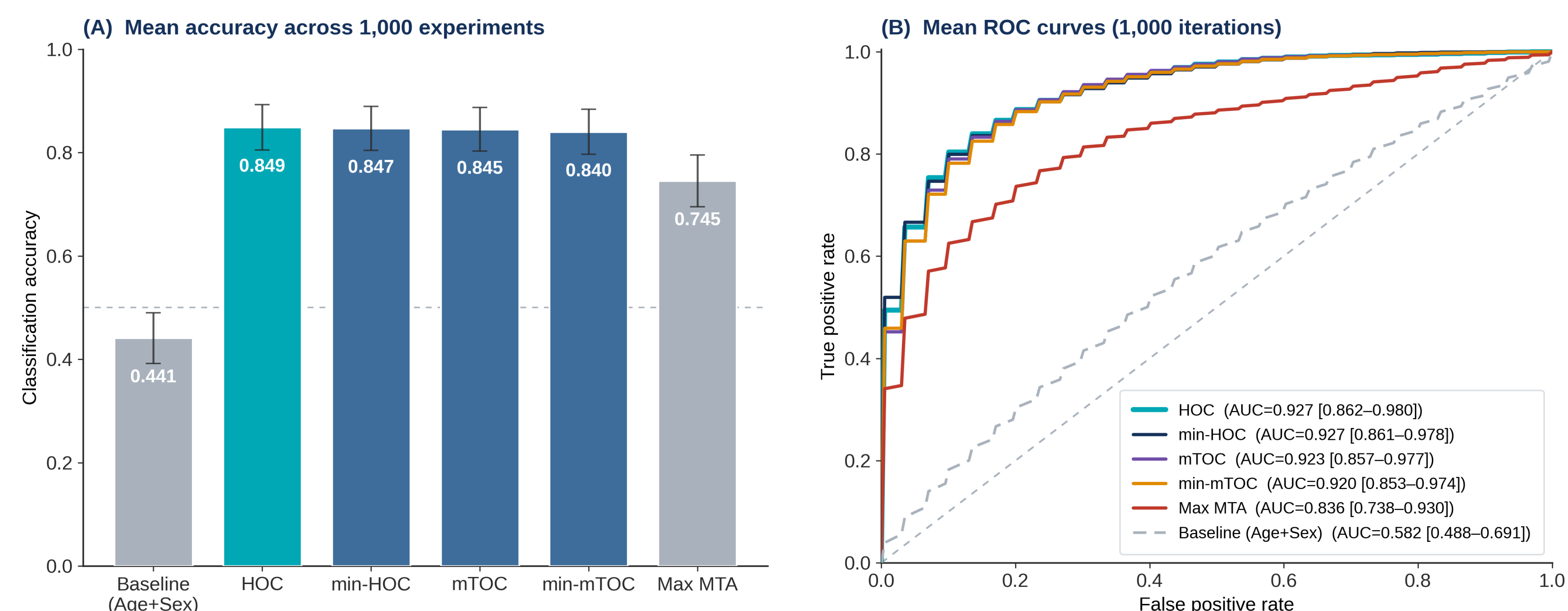


Figure 2. Classification performance of occupancy-index features for AD prediction. (A) Mean accuracy across 1,000 experiments. (B) Mean ROC curves; HOC/min-HOC AUC = 0.927 vs Max MTA 0.836.

03 Results

Group comparison (Table 2)

- All occupancy indices were **significantly lower in AD than CN (all $p < 0.001$)**:
 - HOC: 0.779 ± 0.095 (CN) vs 0.596 ± 0.127 (AD)
 - min-HOC: 0.759 ± 0.101 vs 0.557 ± 0.138
 - mTOC: 0.880 ± 0.060 vs 0.754 ± 0.097
 - min-mTOC: 0.868 ± 0.065 vs 0.724 ± 0.111
- Max MTA distribution shifted higher in AD (grade 4: **35.3% AD vs 2.7% CN**; $p < 0.001$).

Table 2. Occupancy indices and Max MTA grade (CN vs AD)

	CN (N=150)	AD (N=150)	p-value	Total (N=300)
HOC	0.779 ± 0.095	0.596 ± 0.127	<0.001	0.688 ± 0.145
min-HOC	0.759 ± 0.101	0.557 ± 0.138	<0.001	0.658 ± 0.157
mTOC	0.880 ± 0.060	0.754 ± 0.097	<0.001	0.817 ± 0.102
min-mTOC	0.868 ± 0.065	0.724 ± 0.111	<0.001	0.796 ± 0.116
Max MTA			<0.001	
— grade 1	13 (8.7%)	1 (0.7%)		14 (4.7%)
— grade 2	95 (63.3%)	30 (20.0%)		125 (41.7%)
— grade 3	38 (25.3%)	66 (44.0%)		104 (34.7%)
— grade 4	4 (2.7%)	53 (35.3%)		57 (19.0%)

Classification performance (SVM) (Figure 2)

04 Conclusion

- AI-derived occupancy indices provide accurate, objective discrimination of AD from CN and outperform conventional MTA visual scoring.
- Being automated, the approach is reproducible and free of inter-rater variability, supporting its use as an objective atrophy-grading marker.
- Future work: extend the automated grading framework to support clinical diagnosis of early-stage AD and to inform treatment-strategy development.

References

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