

1 BACKGROUND

- Brain atrophy is a core pathological feature of Alzheimer’s disease (AD) and is closely linked to cognitive decline.
- Quantifying **longitudinal brain parenchyma volume loss (BVL)** across the AD continuum with scalable, robust methods remains a key challenge.
- Manual and semi-automated volumetry is labor-intensive and sensitive to scanner and protocol heterogeneity in routine data.
- A fast, validated, deep learning–based biomarker of atrophy could enable large-scale use in **research and clinical trials**.

🎯 OBJECTIVE

Quantify the association between deep learning–derived annual BVL and the rate of cognitive decline (Δ CDRSB/year) across the entire AD continuum.

2 METHODS

■ Population & Data

- All available **T1-weighted MRI** scans across **all ADNI phases**.
- Six diagnostic groups:** CN, SMC, EMCI, LMCI, MCI, AD.
- On average **3.3 ± 1.4 scans** per participant.
- Mean observation period **3.02 ± 1.97 years**.

■ Imaging Biomarker — BrainLossNet

- BVL** computed between consecutive T1w scans using **BrainLossNet**, a fast, robust, validated deep learning method.
- BVL/year** = sum of interval-wise BVL estimates normalized by follow-up duration.

■ Cognitive Outcome

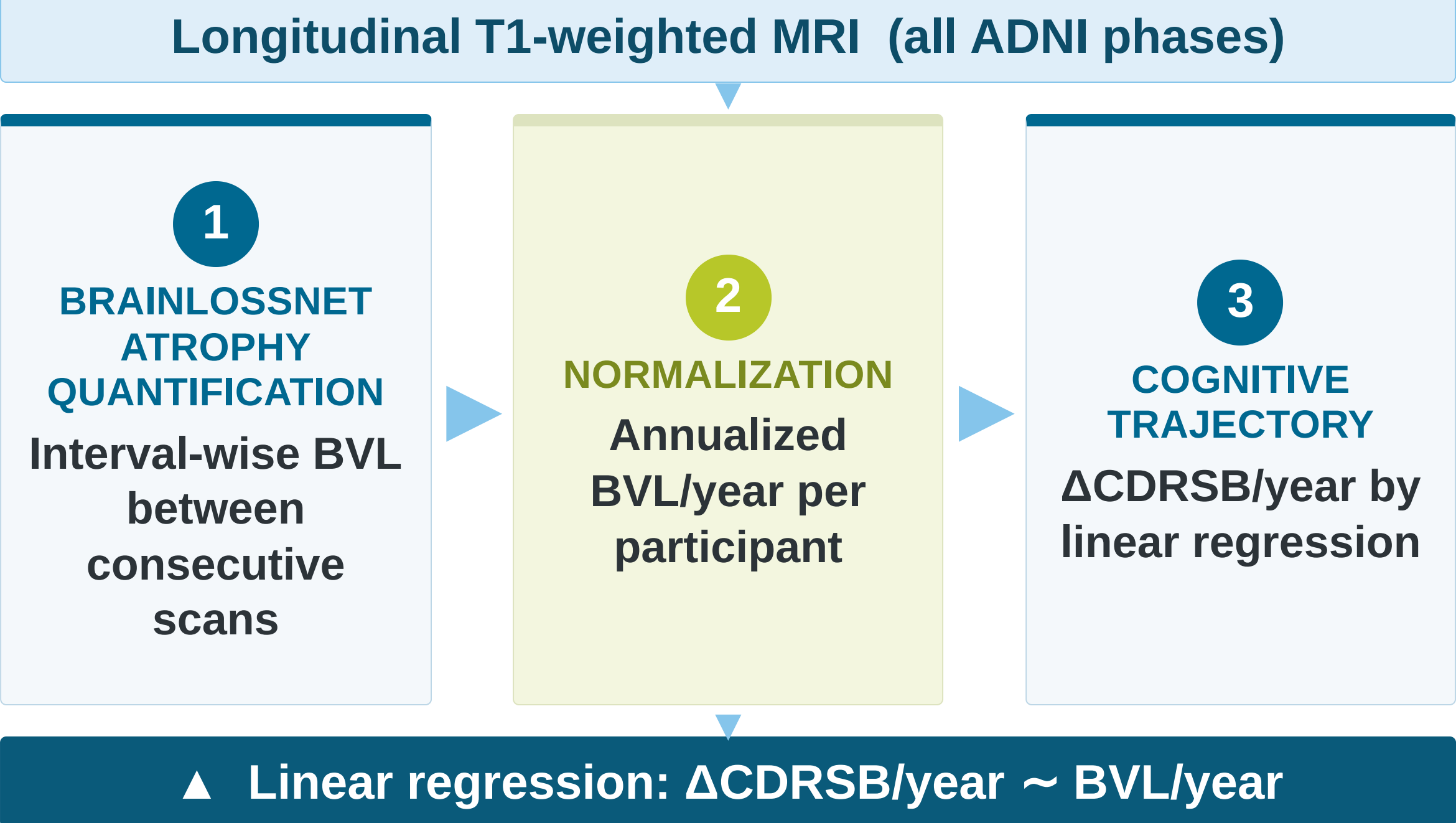
- Δ CDRSB/year**: annual change in Clinical Dementia Rating – Sum of Boxes.
- Estimated by **linear regression** over each participant’s observation period.

■ Statistical Analysis

- Linear regression of **Δ CDRSB/year on BVL/year**.
- Variance explained (**R²**) overall, by group, and over restricted follow-up windows (1 yr, 2 yr).

2 METHODS (CONT.)

■ Analysis Workflow



3 RESULTS

BVL/year vs. Cognitive Decline (Δ CDRSB/year)

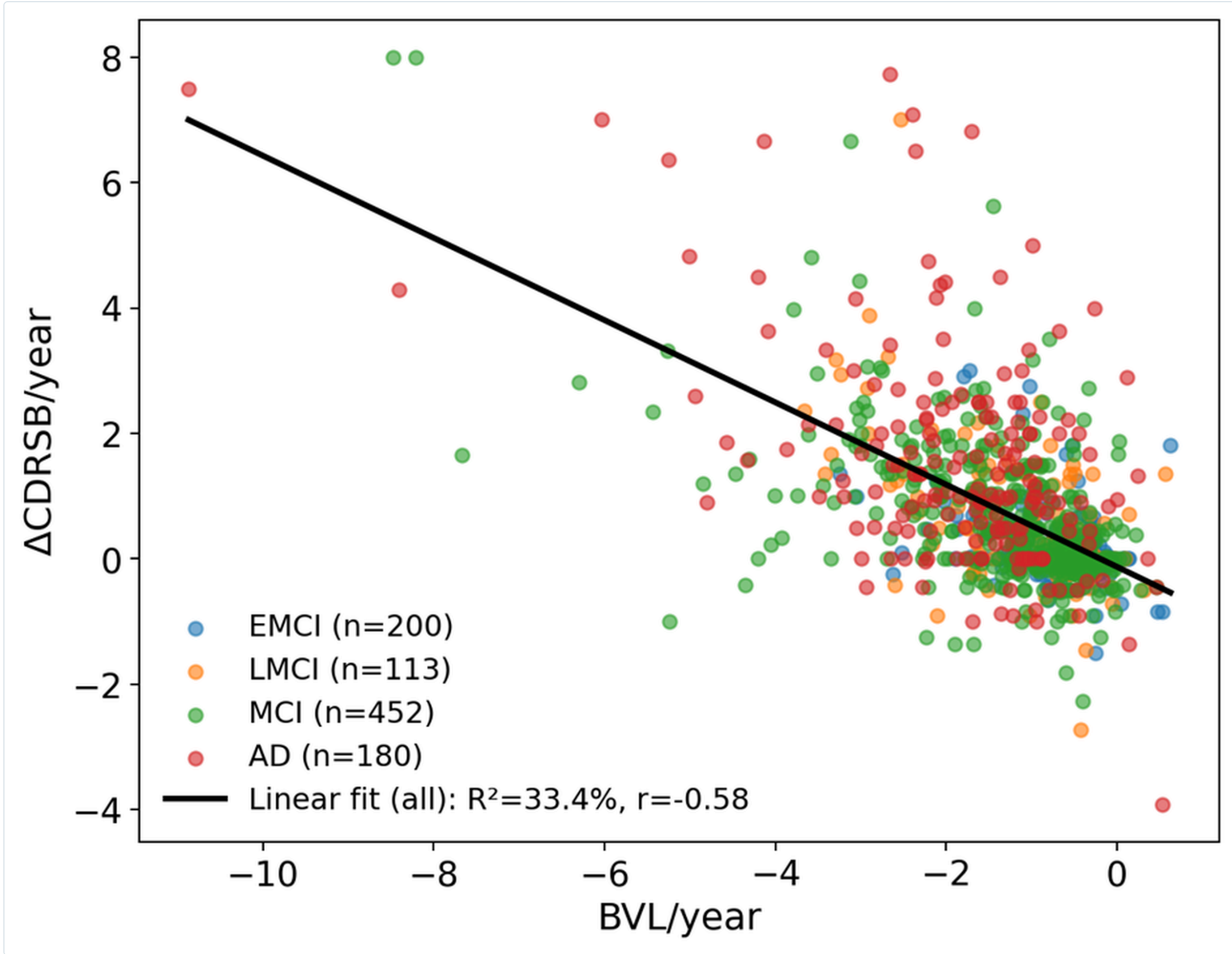


Figure 1. Across the AD continuum (EMCI/LMCI/MCI/AD; n=945), faster annual brain parenchyma loss is associated with faster cognitive decline ($r = -0.58$, $R^2 = 33.4\%$, $p < 0.0001$).

BVL/year and Δ CDRSB/year Rise

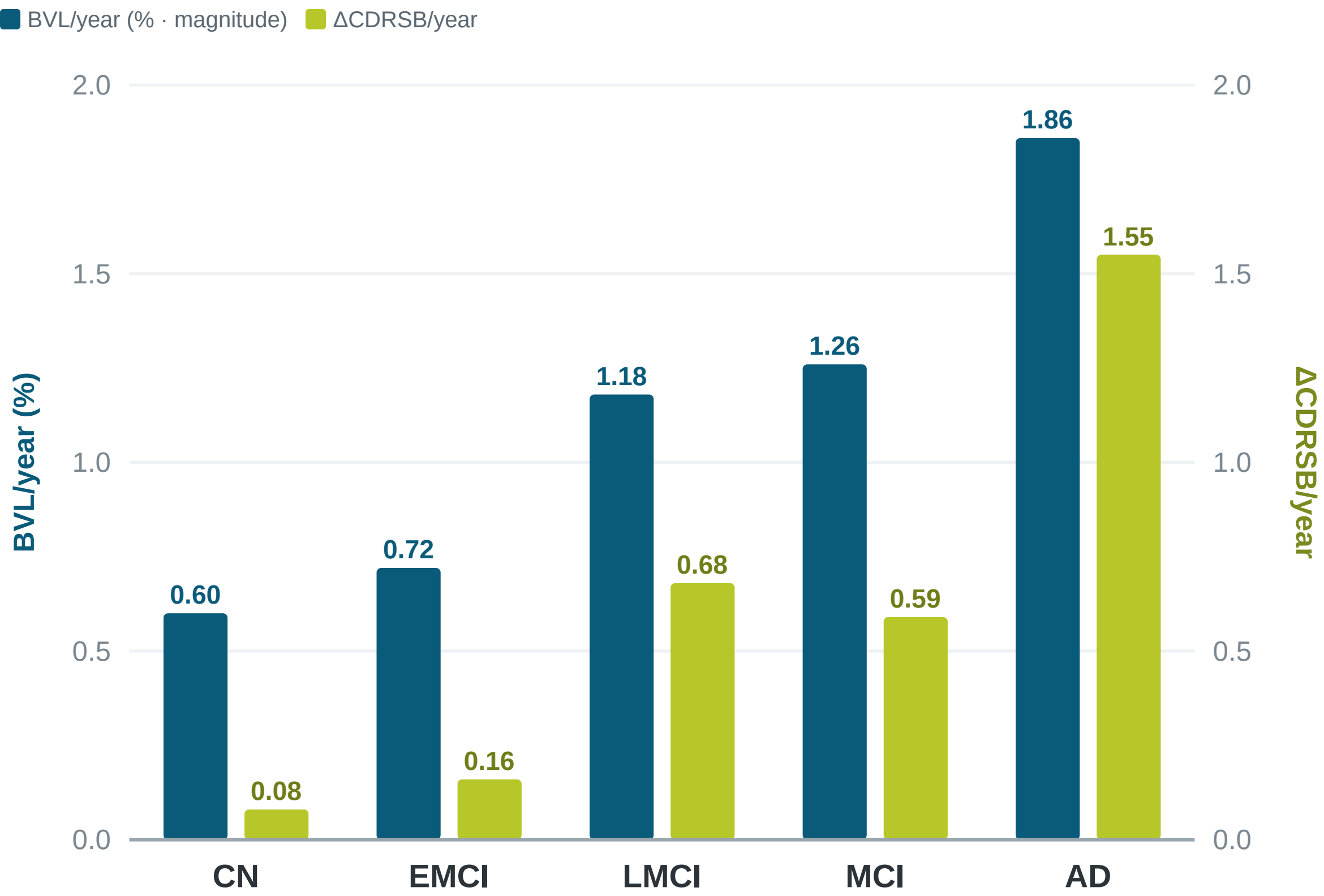


Figure 2. Group-mean annual brain parenchyma loss and cognitive decline increase in parallel from cognitively normal to AD.

3 RESULTS (CONT.)

Variance in Cognitive Decline Explained by BVL/year

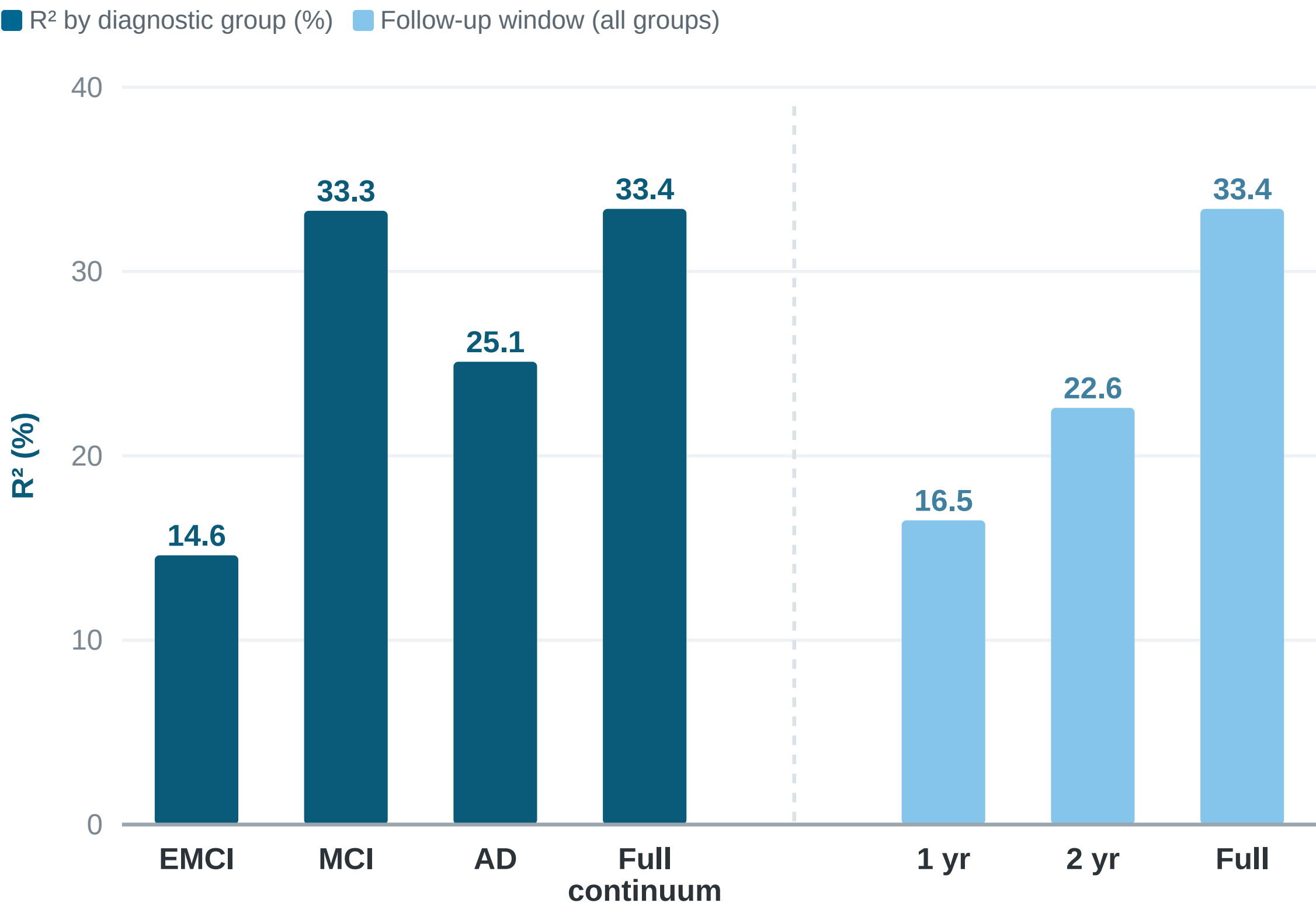


Figure 3. R^2 is highest in MCI (33.3%) and remains highly significant even when restricted to the first year of follow-up (16.5%); all $p < 0.0001$.

★ KEY FINDING

Deep learning–derived **BVL/year** explained **~one third ($R^2 = 33.4\%$)** of the inter-individual variance in cognitive decline across the AD continuum — **33× more than age** (1.0%) — remaining highly significant even when restricted to the first year of follow-up.

4 DISCUSSION

- BVL/year is a **strong, clinically meaningful** predictor of cognitive decline across the AD continuum.
- The biomarker captures decline **early**: explained variance rises from EMCI (14.6%) to MCI (33.3%) and AD (25.1%).
- Effect is **robust over short windows** — $R^2 = 16.5\%$ (yr 1) and 22.6% (yr 2), all $p < 0.0001$ — relevant for trial durations.
- BrainLossNet** enables fast, scanner-robust, scalable atrophy quantification suitable for multi-site data.
- Limitations:** ADNI cohort only; observational design; CDRSB as sole cognitive outcome; no external validation cohort presented here.

5 CONCLUSIONS

- ✓ Annual **BVL** explains **~1/3 of the variability** in CDRSB progression across the AD continuum.
 - ✓ BVL/year vastly **outperforms age** (33.4% vs 1.0%) as a correlate of cognitive decline.
 - ✓ The association is **highly significant even within 1–2 years** of follow-up.
- Clinical & scientific impact**
Deep learning–based BVL is a **scalable imaging biomarker** for AD research and clinical trials — supporting patient stratification, enrichment, and treatment-effect monitoring.

6 CONTACT

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