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Deciphering Longitudinal Anatomical Representations in Brain MRI

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ABSTRACT

Purpose. Longitudinal brain MRI reveals anatomical change associated with aging and neurodegenerative disease, but interpretation is difficult: changes are subtle, anatomy is heterogeneous across subjects, and trajectories vary across diagnostic and cognitive states. Existing approaches rely on population averages or static comparisons, limiting individual-level characterization.

Methods. We encode 3D T1-weighted brain MRI into a multi-scale discrete latent space with a vector-quantized variational autoencoder (VQ-VAE), and model temporal relationships with a latent dynamics model that enforces longitudinal ordering. Subject-level variables (age, sex, diagnosis, MMSE, CDR, FAQ, NPI-Q, GDS, BMI, APOE) enable stratified trajectory analysis. The framework was evaluated on longitudinal brain MRI from ADNI.

Results. Representations were temporally consistent and preserved population-level anatomical trends and region-specific structural variation. Hippocampal and amygdala representations aligned better with known neurodegenerative patterns than baseline longitudinal models. Auxiliary inference models recovered subject-level variables with strong agreement.

Conclusion. Focusing on latent anatomical representations rather than individual scans supports structured interpretation of disease-related structural dynamics across heterogeneous populations.

KEY CONTRIBUTIONS

- Clinical, cognitive, functional, and genetic variables are treated as first-class signals in temporal anatomical modeling.
- Conditioning effects are measured rather than assumed, through auxiliary inference models trained on observed MRI.
- Temporal coherence is enforced directly in a multi-scale discrete latent space.
- Evaluation is transparent and quantitative, moving beyond population-level or purely image-based analysis.

INTRODUCTION

Longitudinal brain MRI provides insight into anatomical changes associated with aging and neurodegenerative disease. However, understanding how brain structure evolves over time remains challenging:

- changes between visits are subtle;
- anatomy is heterogeneous across subjects;
- trajectories vary across diagnostic and cognitive states.

Existing approaches often rely on population averages or static comparisons, which limits their ability to characterize longitudinal anatomical representations at the individual level.

Purpose. To develop a framework for deciphering longitudinal anatomical representations in brain MRI that supports analysis of disease-related structural dynamics.

METHODS AND MATERIALS

Latent encoding. Three-dimensional T1-weighted brain MRI is encoded into a multi-scale discrete latent space using a vector-quantized variational autoencoder (VQ-VAE).

Temporal modeling. A latent dynamics model captures relationships across scans and enforces longitudinal ordering of latent representations.

Conditioning. Subject-level variables are incorporated to enable stratified analysis of anatomical trajectories:

- Demographic: age, sex, body mass index
- Diagnostic: cognitively normal, mild cognitive impairment, Alzheimer's disease
- Cognitive: Mini-Mental State Examination (MMSE)
- Functional: Clinical Dementia Rating (CDR), Functional Activities Questionnaire (FAQ)
- Neuropsychiatric: NPI-Q, Geriatric Depression Scale (GDS)
- Genetic: APOE genotype

Data. Longitudinal brain MRI from the ADNI dataset, used to assess representation consistency and alignment with subject-level variables.

Evaluation. Auxiliary inference models were trained on observed MRI to estimate demographic, cognitive, functional, and biological variables, then applied to MRI-derived representations to evaluate preservation of subject-level information.

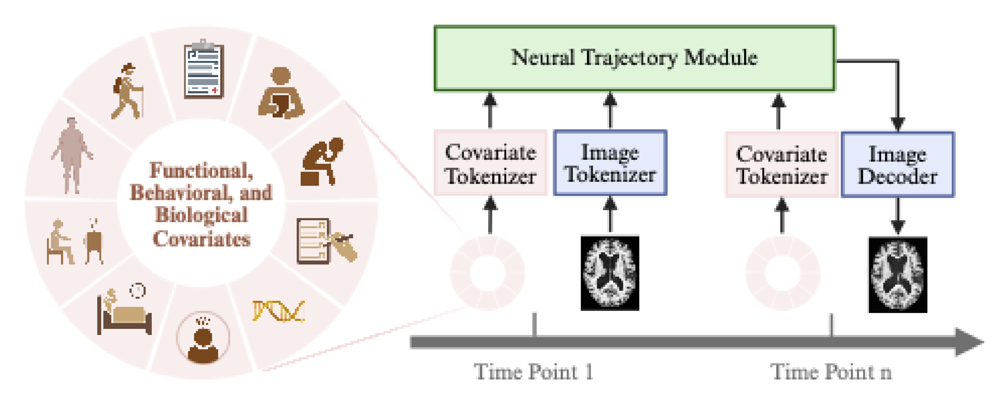

Figure 1. Architecture of the proposed approach. Brain MRI and associated clinical covariates are jointly encoded at each time point, and a latent transition module models subject-specific temporal dynamics conditioned on clinical information.

RESULTS

Temporal consistency. The framework produced temporally consistent longitudinal representations that preserved population-level anatomical trends and region-specific structural variations, indicating capture of gradual structural evolution rather than scan-specific variability.

Region-specific behavior. Hippocampal and amygdala representations showed improved alignment with known patterns of neurodegenerative change compared with baseline longitudinal modeling approaches (Fig. 2).

Condition faithfulness. Inferred covariates agreed strongly with reference values across age, diagnostic category, cognitive performance, and functional measures (Fig. 3), indicating that the learned representations maintained meaningful associations with subject-level characteristics.

Comparison with baselines. The proposed framework exhibited stronger alignment between anatomical features and subject-level variables across multiple dimensions, suggesting enhanced preservation of clinically relevant anatomical information over time (Figs. 2, 3).

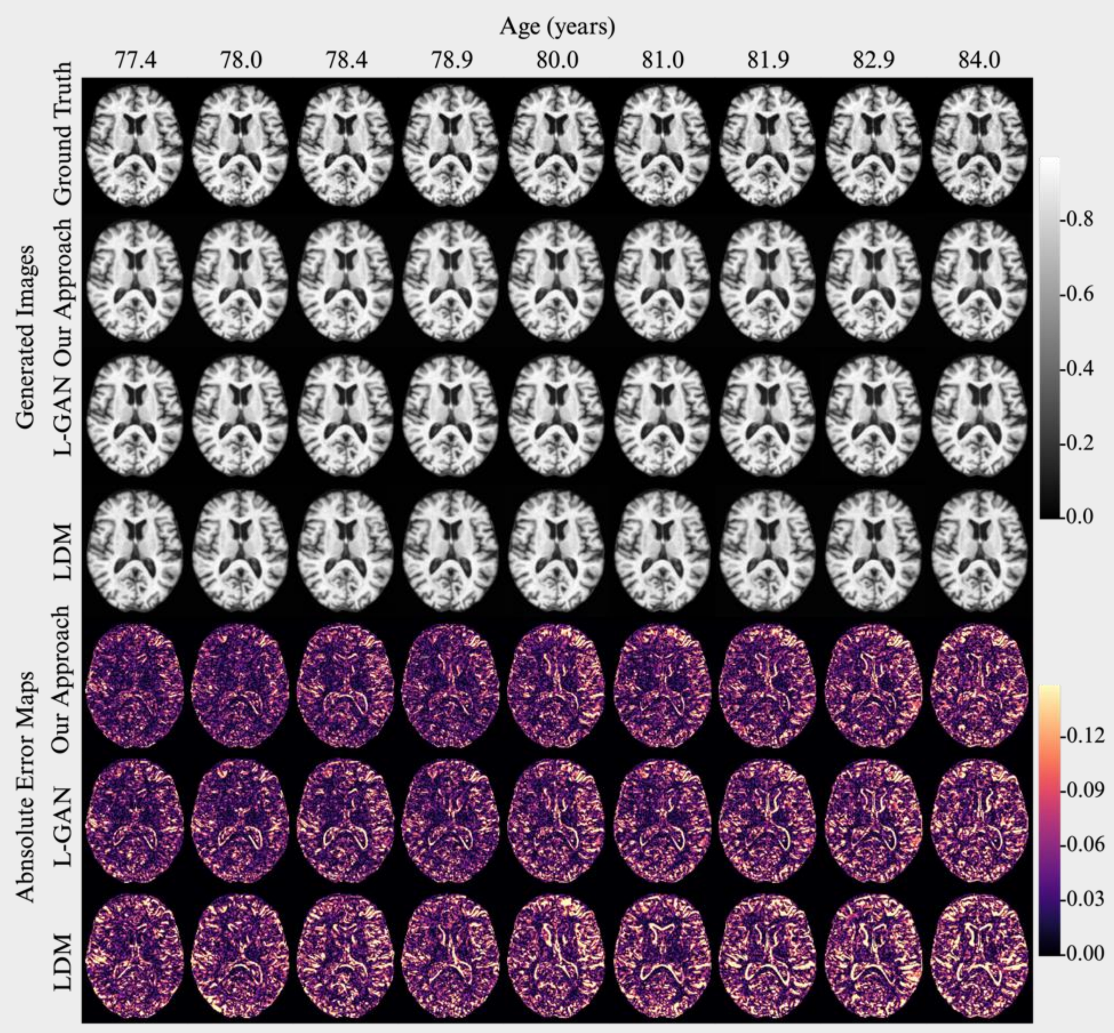

Figure 2. Longitudinal brain MRI slices across increasing age. The top rows show reference images, followed by corresponding results from different modeling approaches. The bottom rows display voxel-wise absolute differences, illustrating how anatomical changes evolve over time and where deviations occur.

DISCUSSION

Conditioning as a first-class signal. The framework treats subject-level clinical, cognitive, functional, and genetic variables as first-class signals within temporal anatomical modeling, rather than as auxiliary side information.

Measuring, not assuming, conditioning effects. Rather than assuming that conditioning variables meaningfully affect learned anatomical features, the framework explicitly tests this assumption through an auxiliary inference–based evaluation strategy. Independent models trained on observed MRI are used to probe longitudinal anatomical features, directly assessing whether subject-level information is preserved and reflected over time.

Toward measurable conditioning. This shifts longitudinal neuroimaging analysis from implicit conditioning toward measurable, interpretable conditioning effects, emphasizing controlled incorporation of subject information, temporal coherence, and transparent evaluation of model behavior.

Scope. Analyses are based on ADNI; extension to independent cohorts is a direction for future work.

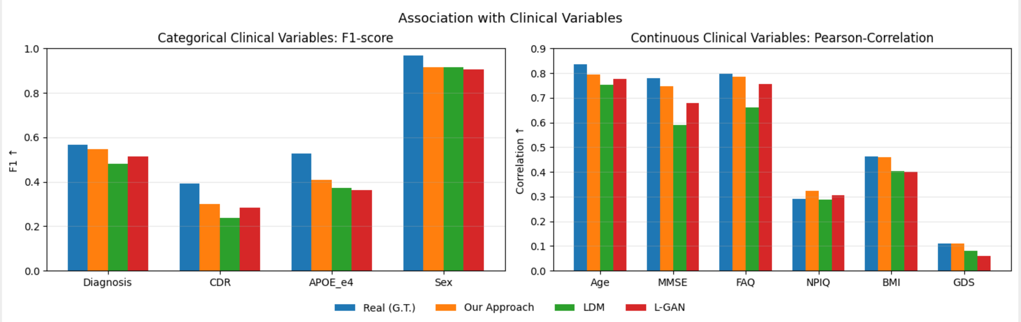

Figure 3. Association between brain MRI–derived features and clinical variables, evaluated using auxiliary inference models trained on observed imaging data. Higher values indicate stronger preservation of clinical information.

CONCLUSIONS

This work introduces a representation-based framework for analyzing longitudinal brain MRI that enables structured interpretation of anatomical evolution over time.

By focusing on latent anatomical representations rather than individual scans, the approach supports investigation of disease-related structural dynamics across heterogeneous subject populations, while providing an interpretable and quantitative means of assessing how subject conditions influence longitudinal modeling.

ACKNOWLEDGMENTS

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