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BIOMARKERS

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NEUROIMAGING

Representing the Cognitive Impairment Continuum of Alzheimer's Disease and Lewy Body Dementia with a Novel Finer-Scale Cortical Representation via Disease Embedding Tree

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Abstract

Background: Alzheimer's Disease (AD) and Lewy Body Dementia (LBD) often exhibit overlapping neuropathological features and symptoms, posing significant challenges for differential diagnosis. While many studies focus on leveraging machine learning with neuroimaging data for early dementia diagnosis, investigating the progression and interactions between AD and LBD offers an opportunity to uncover valuable insights into their shared features and hidden connections.

Method: We propose the Disease Embedding Tree (DET) framework to model continuous relationships among AD, Cognitively Normal (CN), and LBD subjects on T1-weighted structural MRI data from 106 subjects (36 AD: 15 females, 21 males; 78.25 ± 5.76 years; 35 CN: 15 females, 20 males; 76.74 ± 5.15 years; 35 LBD: 8 females, 27 males; 78.37 ± 6.94 years).

For each subject, we reconstructed cortical surfaces and adopted a novel cortical folding pattern representation, Gyral Network, to identify the potential cortical hubs, known as 3 hinge gyri (3HGs). Cortical features, including cortical thickness, curvature, sulcal depth, fractal dimension, and local gyrification index, were extracted from 3HGs and used to train the DET model.

The DET model projects the extracted features of each subject to a high-dimensional embedding space. The order constraint conditions the inter-group relationship while the Mini-Mental State Examination (MMSE) scores are incorporated to model the inter-subject continuous relationship in embedding space, shown in Figure 1. Additionally, our model supports the classification task based on the proximity of the subjects in the embedding space, providing both continuous relationship and diagnostic capability.

Result: The DET framework has achieved superior performance on the classification task across all the evaluation metrics compared to the traditional machine learning based methods, as demonstrated in Table 1. Figure 2 shows that the CN, AD patients, LBD patients are projected to the DET based on the learned representations in the embedding space.

Conclusion: The DET framework effectively models the continuous relationships among CN, AD, and LBD subjects and outperforms the traditional models in the classification task. By leveraging cortical features of the cortical hubs and the MMSE-based constraints, it provides valuable insights into disease progression.

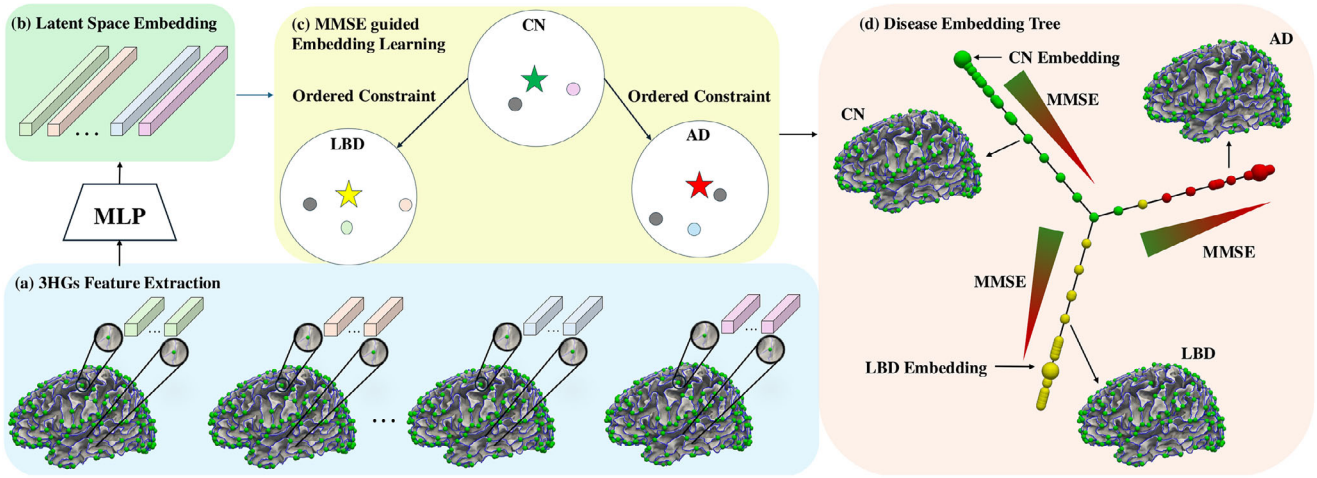

Fig. 1. Method Overview. The proposed Disease Embedding Tree framework integrates cortical surface features with cognitive assessment (MMSE scores). First, we extract 3HG features (a) and project them into a latent space embedding (b). Next, we apply the tree model to learn these embeddings (c) and construct a tree (d) that visualizes MMSE scores for each subject, effectively illustrating cognitive impairment levels across the tree structure.

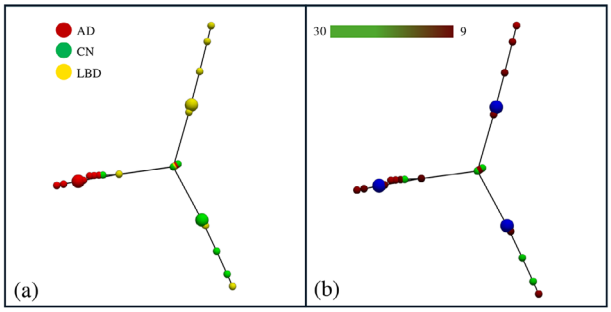

Fig. 2. DET generated from the test dataset. Fig. 2(a) shows clusters based on disease stages AD, CN, and LBD and Fig. 2(b) displays MMSE score of the corresponding test subjects, where color gradients represent cognitive impairment levels from normal cognitive (green) to severe cognitive impairment(red).

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Model	Acc(%)	Pre.(%)	Re.(%)	F1(%)
SVM (Linear)	61.90	65.48	61.90	61.60
SVM (RBF)	61.90	65.56	61.90	62.34
Logistic Regression	57.14	57.41	57.14	56.73
Random Forest	66.67	70.90	66.67	67.66
KNN	52.38	69.05	52.38	41.27
Disease Embedding Tree	72.41	73.01	72.41	71.88

Table 1. The best performance of classifying AD, CN, and LBD with different machine learning models