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Paper

Early Prediction of Alzheimer's Disease Progression Using Variational Autoencoders

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Introduction

- Using MRI: capture in vivo morphological brain changes in AD
- Using computational techniques: detect more subtle and informative quantitative changes
- **Aim:** predict a subject's future Alzheimer's disease progression from their structural MRI (sMRI).

- Use variational auto-encoder (VAE): produces latent variables which are probabilistic and can be sampled.
- Leverage these variables in two different ways :

1. visualize the areas of the brain
2. quantify the distribution of possible disease evolution paths for a given patient, produce an empirical risk measure

Related Work

Existing Methods

- Bayesian models
- Sparse Inverse Covariance Estimation methods
- Fused features to train a classifier based on SVM and LDA
- Extracted neural network-based features from multiple modalities
- Convolutional Neural Networks

Problems

- requirement of multiple diagnostic tests imposes a financial burden
- CNN do not produce actual identifiable biomarkers

Method

an MRI taken at time step t by $\mathbf{x_t} \in \mathcal{R}^{D \times H \times W}$

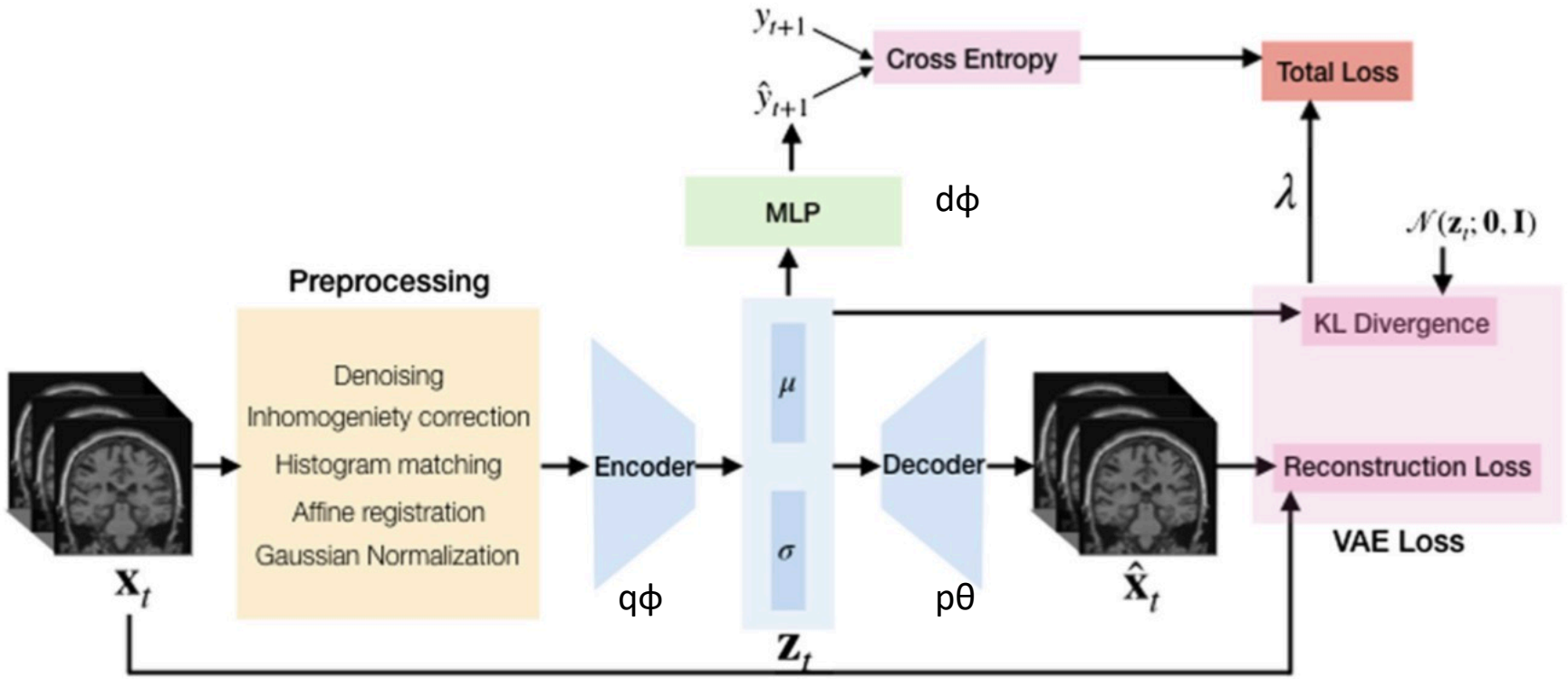

Fig. 1. Flow diagram for training.

Objective of MLP

- minimize loss

$$\mathcal{L}(\phi, \theta, \varphi; \mathbf{x}_t, \mathbf{y}_{t+1}) = \mathcal{L}_{CE} + \frac{\lambda}{2} \sum_{j=1}^{J} \left(1 + \log \sigma_j^2 - \mu_j^2 - \mu_j^2 - \sigma_j^2 \right) + ||\mathbf{x}_t - \hat{\mathbf{x}}_t||_2^2$$

J is the latent dimension and $\hat{\mathbf{x}}$ the reconstructed image.

calculate $p(\hat{y}|\mathbf{x}; \phi, \varphi)$ to predict the probability of the disease progression.

Experiment

Data

- Dataset: 1.5 T1-weighted sMRI from ADNI dataset, size 233 × 197 × 189
- All images went through a preprocessing pipeline
- Eventually, image intensities were normalized within each image and among the whole database.
- 4046 MRIs from 1092 patients, split the data into 8:1:1 ratio at the patient level. Training, validation and test set consists of 3257, 396 and 393 MRIs from 873, 109 and 110 patients, respectively. In the test set, 145 out of 393 are diseased.

Implementation: CNN-AE

- Discriminative baseline: trained a 3D CNN with binary cross-entropy loss
- Second baseline: regularized the CNN with the reconstruction loss.
- （Adam Optimizer）

- The encoder consists of four 3D CNN layers,
- The decoder consists of four transposed CNN layers,
- The dimension of the latent space is 1024.
- The MLP is composed of two fully connected layers with 4096 dimensions followed by a classification layer.

Results

Classification Performance

Table 1. Performance on the test set.

Model	Parameters	Accuracy	F1-score	Cross-entropy
CNN	97.34M	77.35%	0.71	0.48
CNN-AE	98.43M	81.93%	0.78	0.46
VAE	74.9M	$74.40 \pm 0.01\%$	0.66	0.73

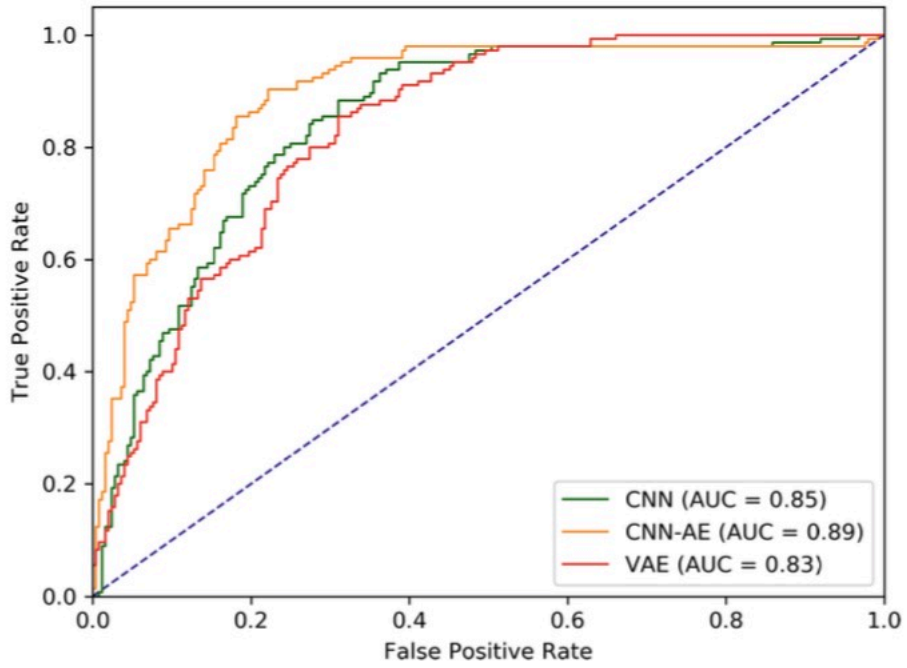

Fig. 3. Test set ROC curve.

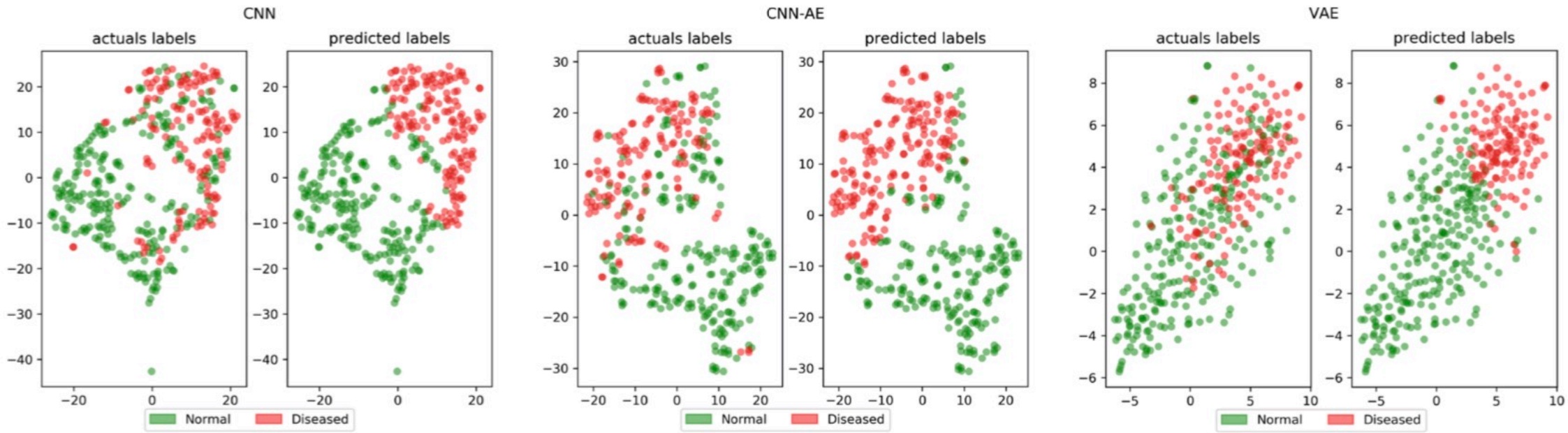

Fig. 2. Pre-activation t-SNE embedding of thee final layer of the classifier on test set. 2 principal components are visualized.

Risk Analysis

Table 2. Percentage risk of currently healthy patients, based on 100 sample prediction on each MRI in the test set.

Risk band	VAE	CNN	CNN-AE
0	59.27%	2.79%	9.16%
1–19	16.13%	32.82%	29.51%
20–39	5.24%	11.19%	9.16%
40–59	2.42%	21.12%	15.52%
60–79	2.82%	22.90%	23.16%
80–100	14.11%	9.16%	13.49%

- Extracted the patient data which had labels for timestep t + 2
- No example of disease progression from healthy to diseased state
- Prediction of the VAE is closer

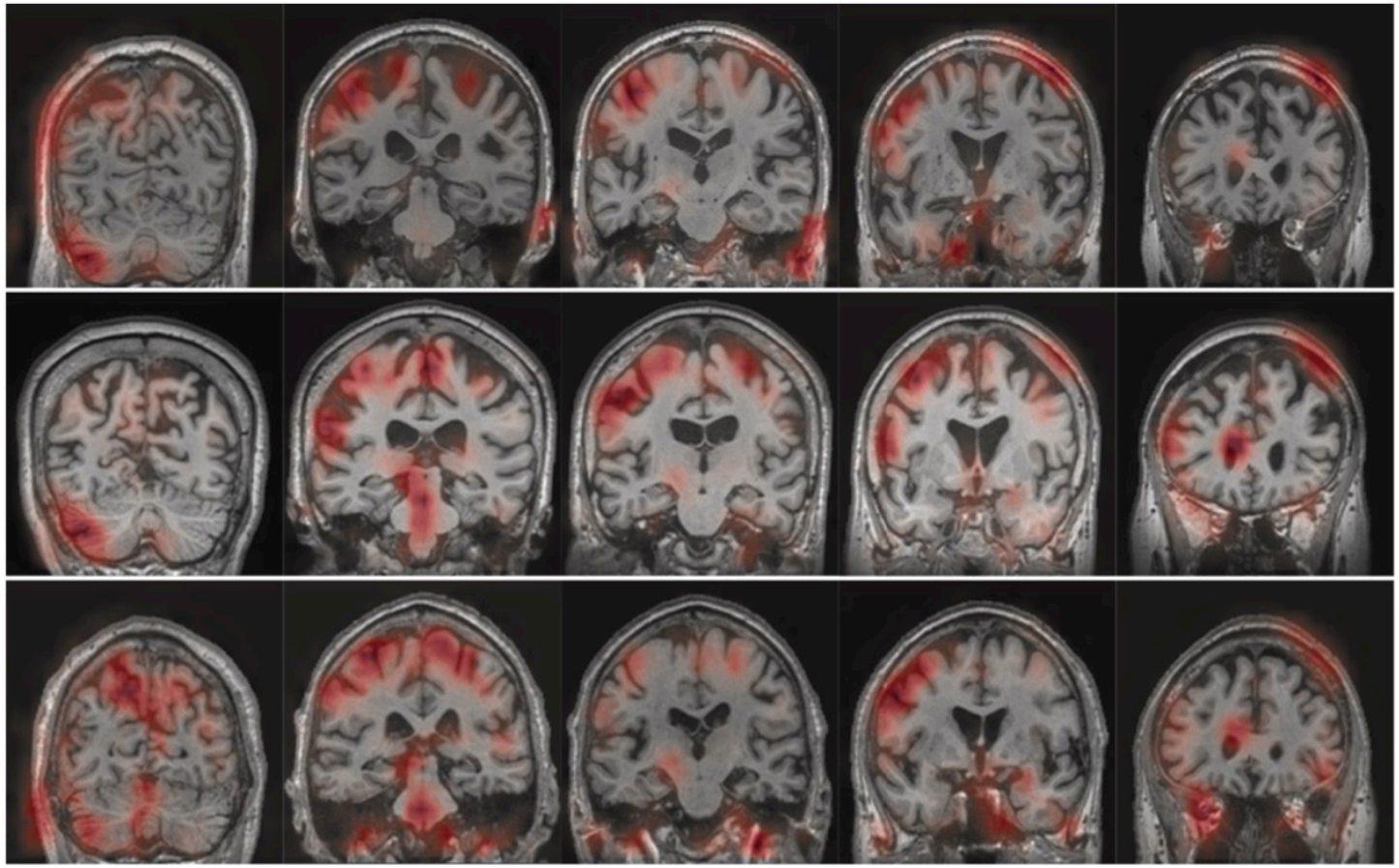

Fig. 4. Relevance maps for 3 subjects. Row 1: HL at baseline, HL at follow-up, row 2: HL at baseline, AD at follow-up, row 3: AD at baseline, AD at follow-up. Consistent areas of relevance include cerebellum (column 1), neocortex (columns 2–4) and brain stem (column 2).

Qualitative Results

- visualized the 3D relevance map of the final encoder layer conditioned on the input MRI

The model appears to be focusing on specific areas of the neocortex, cerebellum and brainstem.

The hippocampus and entorhinal cortex did not emerge as areas with high relevance.

Limitation & Future

- These maps are regionally specific but give no indication of what features the network is identifying in these areas.
- Future work is necessary to explore in more detail how the cerebral anatomy is changing.
- Data-driven maps are useful to corroborate existing targeted neuroanatomical markers in AD and to highlight areas for further research.

Conclusion

- VAEs are a promising alternative to predict early the potential AD progression.
- The potential of this approach to detect healthy patients which may require close follow-up
- Future directions: learning a predictive model based on past image acquisitions, reminiscent of recent work on video generation or segmentation of ambiguous medical images.

Source

- Paper Link: https://rdcu.be/bT8Yt
- Code: https://github.com/sumanabasu/CNN-in-tracking-Alzheimers