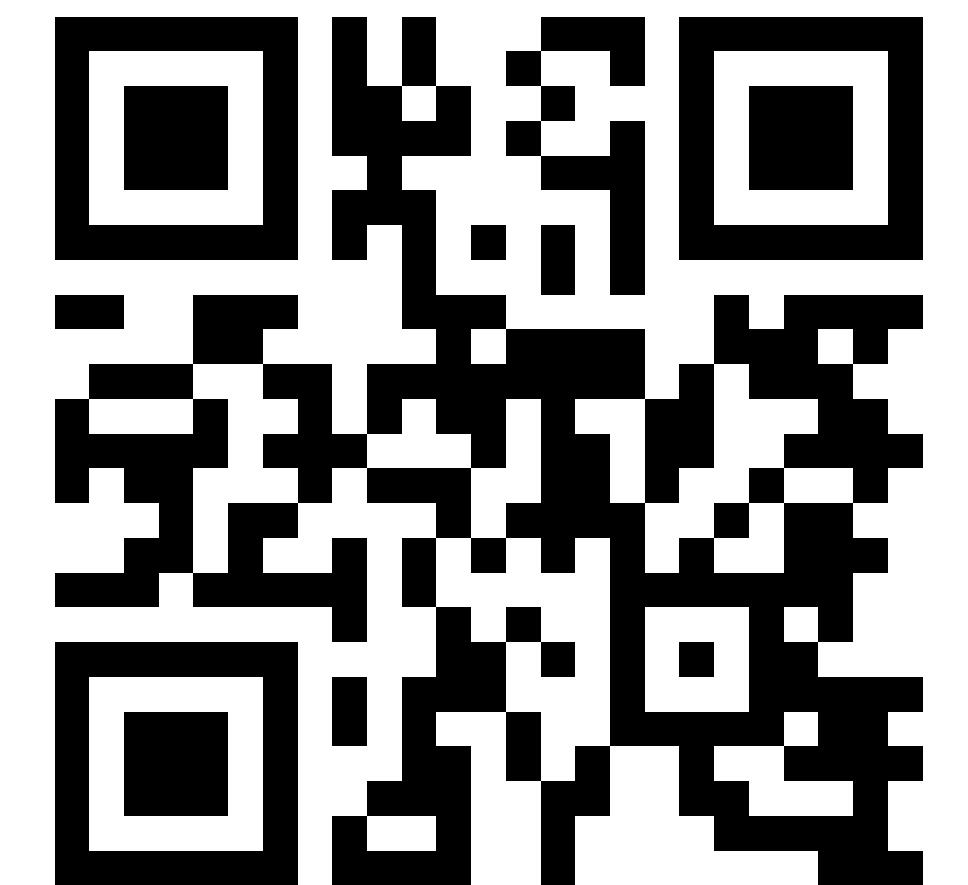


Early Prediction of Alzheimer's Disease Progression using Variational Autoencoders



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Overview

Motivation:

- Alzheimer's Disease (AD) is typically diagnosed from the symptoms of the disease (Mini Mental State Examination Score), rather than the structural changes in the brain.
- The pathological changes in the brain start decades before the manifestation of the symptoms.

Assumption:

Magnetic Resonance Imaging (MRI) is capable of capturing the complex changes in the brain, even if it is difficult for humans to extract those features from the low contrast, multi-dimensional MRIs.

Contribution:

- We built a prototype that predicts how likely a healthy person is to be affected by AD in the near future from sMRI.
- Visualized the potential biomarkers for early prediction of AD.

Method

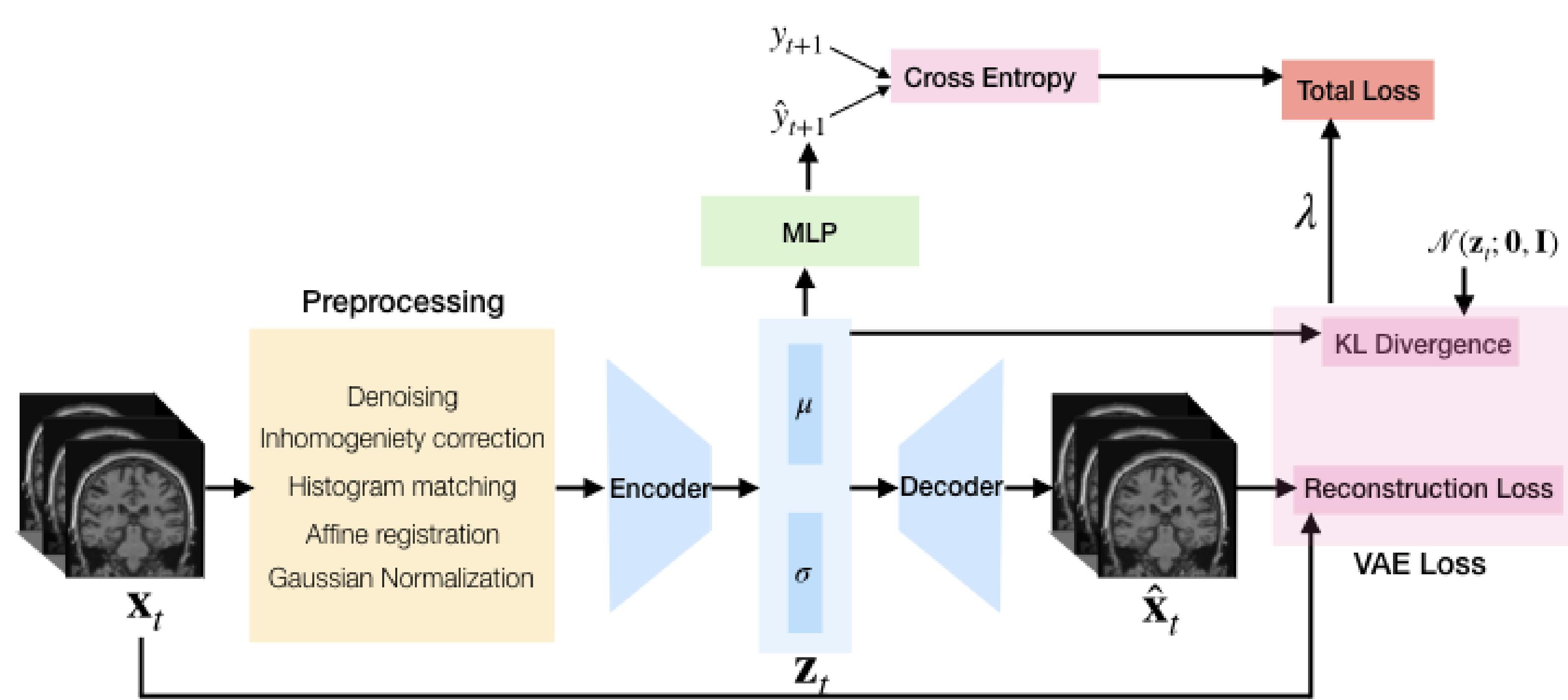


Figure: Training Flow

Our Contribution

Risk prediction with VAE

What is risk?

Empirical probability of a healthy person getting diagnosed with either Mild Cognitive Impairment (MCI) or AD at the next time point.

Why is it difficult to predict?

Deterministic models fail to capture that a patient might evolve in various ways from their current physiological state.

What solution do we propose?

Generative classifiers model the distribution over possible disease progressions, providing a measure of risk for each patient. We propose to use Variational Autoencoder (VAE) [1] to learn a posterior distribution, from which we can sample multiple times to assess the risk.

How do we train**?

Minimize:

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

Results*

Quantitative Results

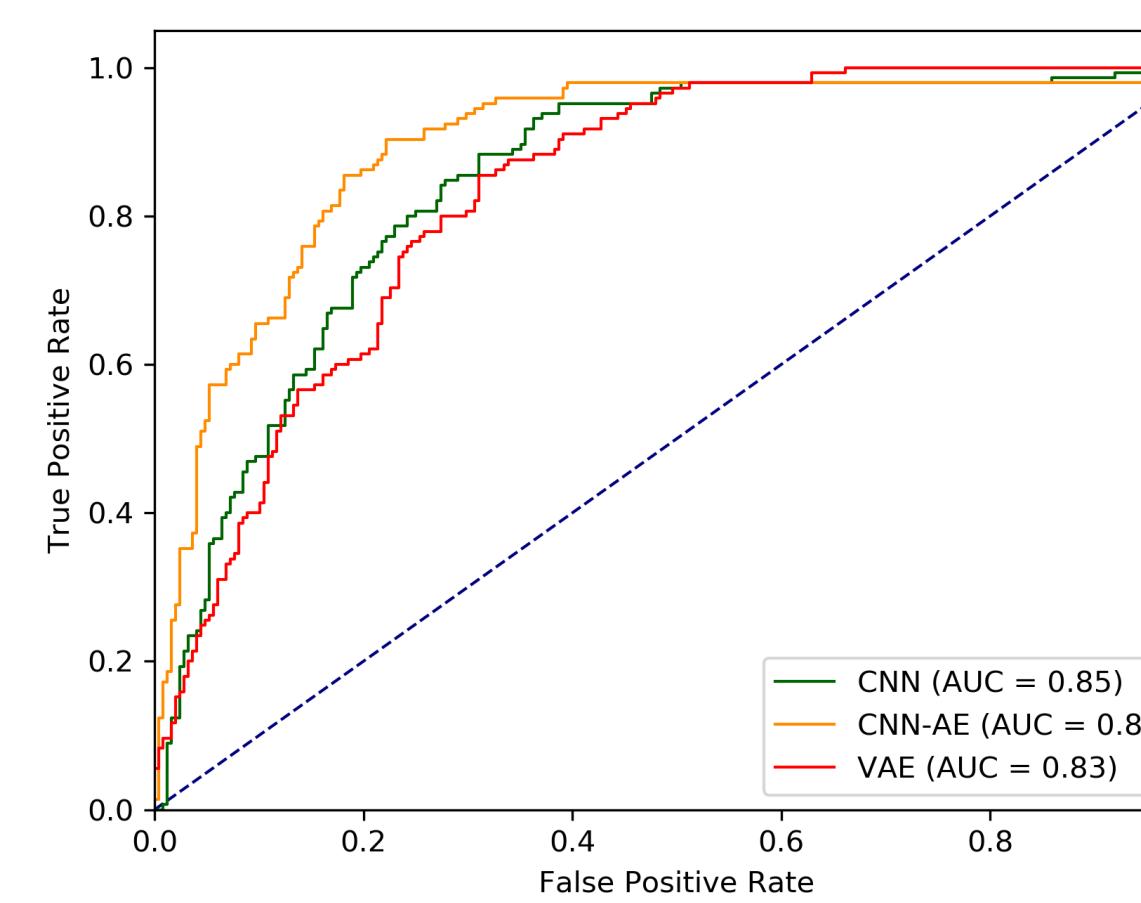


Figure: Performance Analysis: Test set ROC Curve.

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%

Table: Risk Analysis: Percentage Risk of Currently Healthy Patients, based on 100 sample prediction on each MRI in the test set.

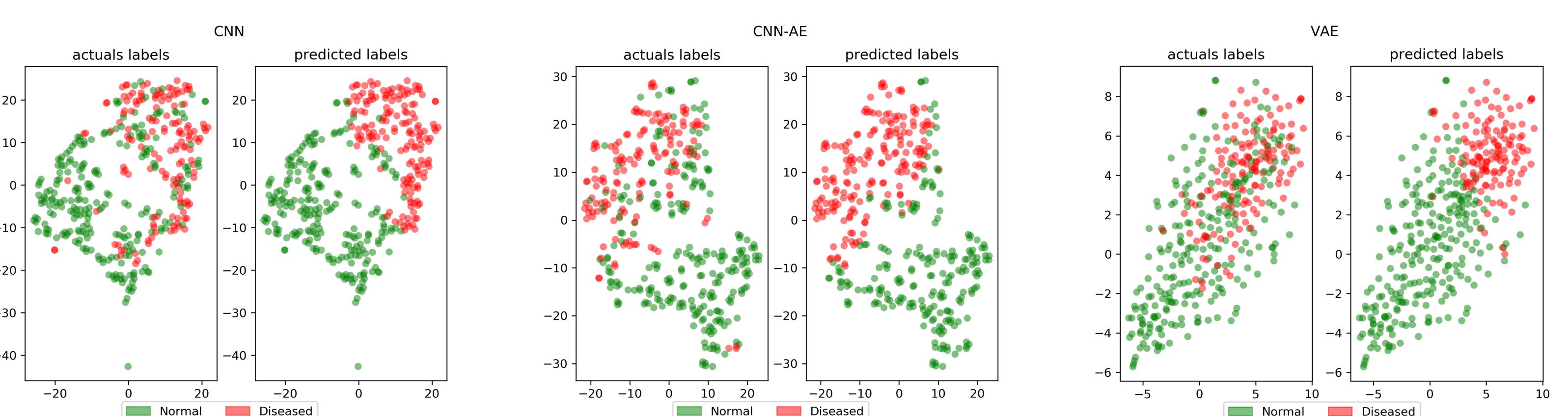


Figure: Pre-activation t-SNE embedding of the final layer of the classifier on test set. 2 principal components are visualized.

Qualitative Results

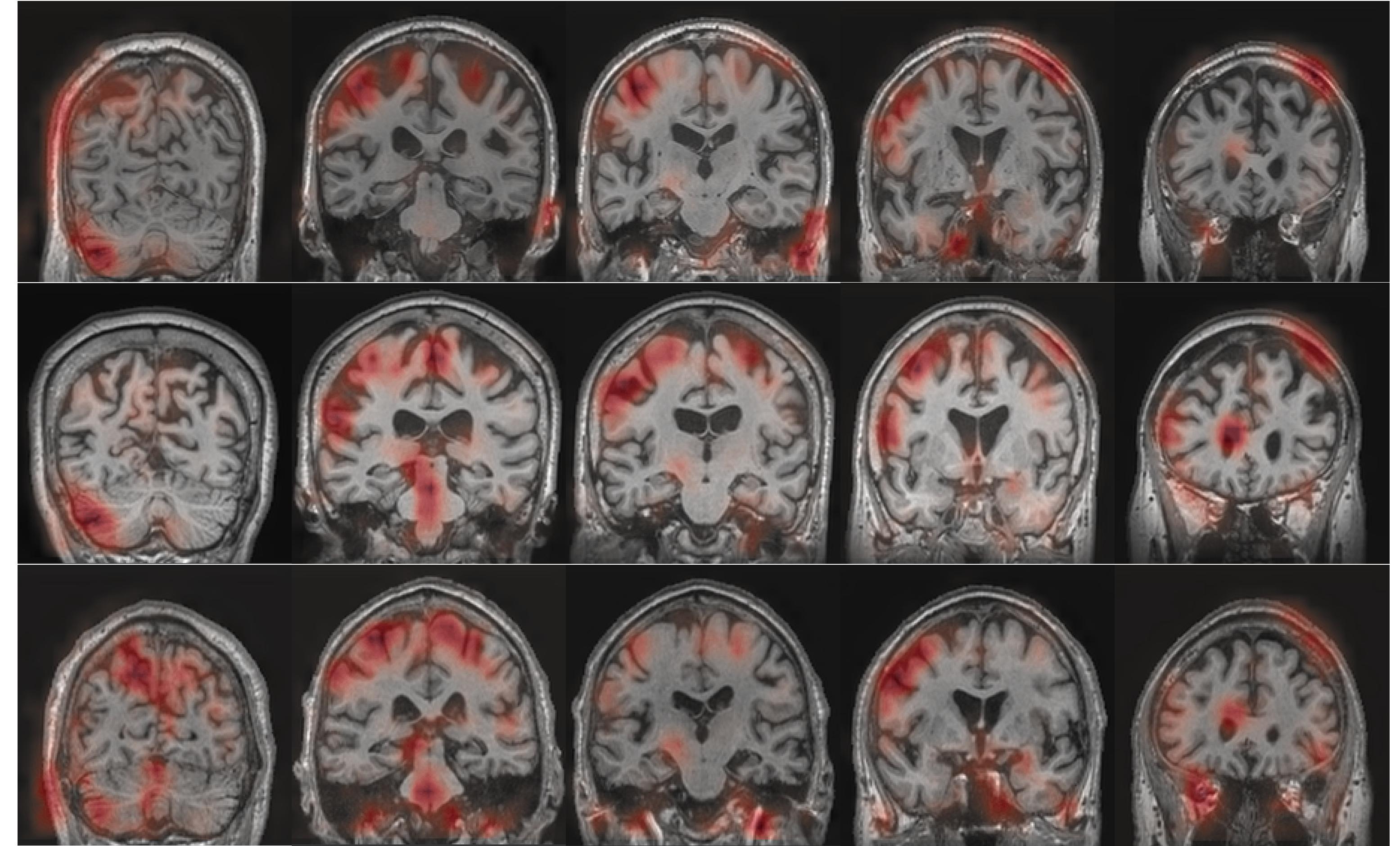


Figure: Relevance maps for 3 subjects. Row 1: HL at baseline, HL at follow-up, row 2: HL at baseline, AD at follow-up, row 3: AD at baseline, AD at follow-up. Consistent areas of relevance include cerebellum (column 1), neocortex (columns 2-4) and brain stem (column 2).

Conclusion & Future Work

- VAEs are a promising alternative for early prediction of potential AD progression.
- Our approach has the potential to detect healthy patients who might require close follow-up.
- Future direction includes training similar models on skull stripped images and further validation of this model on other, larger datasets.

References

- [1] D. P. Kingma and M. Welling, "Auto-encoding variational bayes," *ICLR*, 2013.
- [2] S. G. Mueller *et al.*, "Alzheimer's disease neuroimaging initiative," *Neuroimaging Clinics North America*, vol. 15(4):869-xii, 2005.