Model-based clustering using generative embedding

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1 Introduction

• An important problem in psychiatry is the lack of diagnostic classifications that are based on pathophysiological mechanisms rather than symptoms.

• It is conceivable that one could solve this problem by constructing generative models of brain function that enable inference on the computational and neuronal processes that underlie an observed collection of symptoms.

• We recently showed that generative embedding based on such models can yield highly accurate predictions of a symptom-based diagnostic state from fMRI data [1].

• In this study, we are beginning to address the open question of whether generative embedding might also allow us to discover clinically relevant conditions when such conditions are not known a priori.

2 Datasets

Synthetic fMRI data (n = 80)

Empirical fMRI data (n = 83)

To assess the empirical validity of our approach, we analysed fMRI data from schizophrenia patients and healthy controls engaged in a working memory task [4]. Using a DCM of prefrontal and parietal activity, we asked whether we could discover the diagnostic category 'schizophrenia' from patterns of connectivity.

3 Model-based clustering

We introduce generative embedding for model-based clustering using a combination of dynamic causal models (DCM) and variational Gaussian Mixture Models (GMM) clustering [5].

4 Results on synthetic fMRI data

Our analysis discovered the correct number of clusters (two) when the groups were well separated or there was a sufficiently high signal-to-noise ratio.

5 Results on empirical fMRI data

Using a linear support vector machine (SVM), we were able to predict a subject's diagnostic status with an accuracy of 78% (left). We then adopted an unsupervised exploratory approach: generative embedding inferred that the data comprised two subgroups. These subgroups showed a 71% correspondence with schizophrenic patients and healthy controls (right).

Model-based solutions can be interpreted in terms of the underlying generative model. In the model underlying cluster 1, which contained almost exclusively healthy controls, working memory had a significantly stronger modulatory effect than in cluster 2, which was mostly composed of patients.

6 Conclusions

• Clustering using generative embedding may enable us to decompose groups of patients with similar symptoms into pathophysiologically distinct subtypes.

• In contrast to conventional activation-based, correlation-based, or symptom-based clustering schemes, our approach exploits discriminative information encoded in 'hidden' physiological quantities such as synaptic connection strengths.

• Critically, generative embedding enables a mechanistic interpretation of the discovered structures.