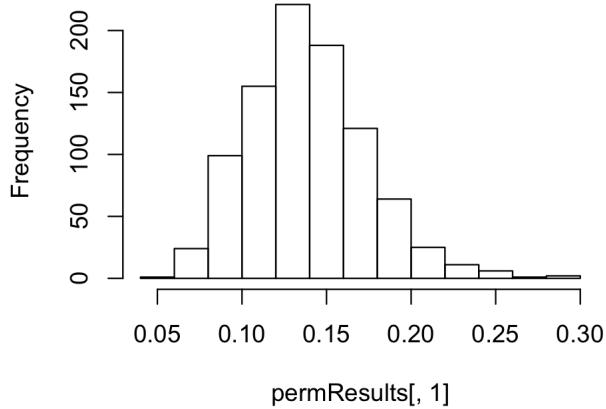


# Software for learning multi-view brain embeddings and application to testing a genotype-phenotype hypothesis in depression: Supplemental analyses

*Brian B. Avants et al.*

10/21/2018

**Depression - Max: 0.284 Mean: 0.138**



**Anxiety - Max: 0.3 Mean: 0.191**

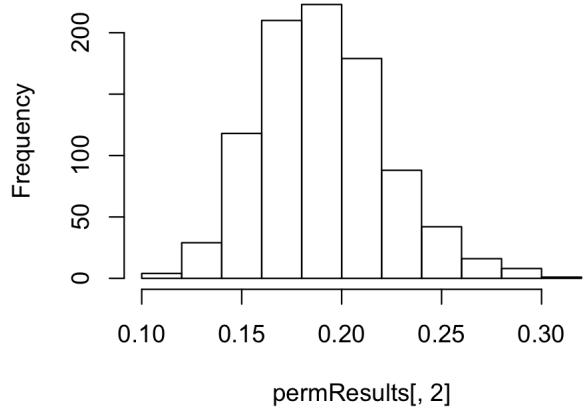


Figure 1: Histogram of results over 1000 permutations. No instances of the permuted data model produced  $R^2$  that exceeded the real data (0.31 and 0.32 respectively)

## Histograms for permutation results

We permuted the input matrices and re-ran the modeling steps with fixed sparseness values. The omnibus model's base parameters (age, gender, GAF, scanner type, etc) were not permuted. Only the embedding parameters were resampled. The distribution of results is centered around 0.14 for depression and 0.19 for anxiety. The tails did not reach the unpermuted model fit in any resampling run.

## Comparison with SVD

The reviewer requested a comparison between SyMILR and SVD performed on the same dataset and with analogous study design. The figures below summarize the omnibus model relationships between the low-dimensional thickness, FA and SNP embeddings produced by SVD and each of the anxiety and depression clinical scores. Both models produce  $R^2$  of 0.23.

### real vs pred: PHX\_ANX\_TOTAL

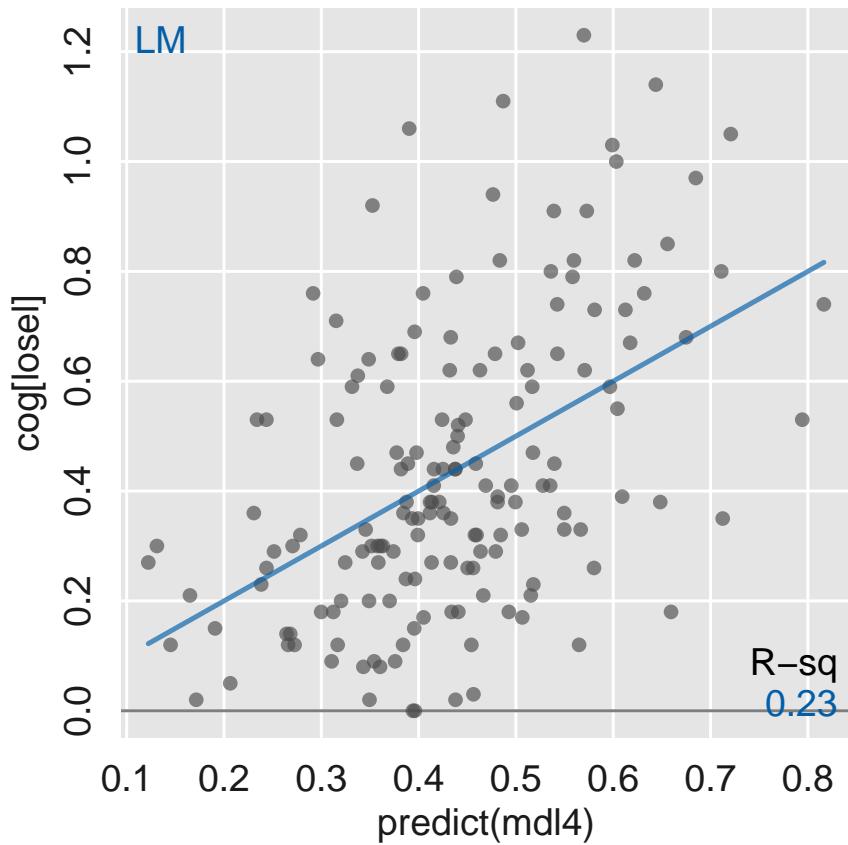


Figure 2: SVD Anxiety

SVD-based prediction of anxiety

### real vs pred: PHX\_ANX\_TOTAL

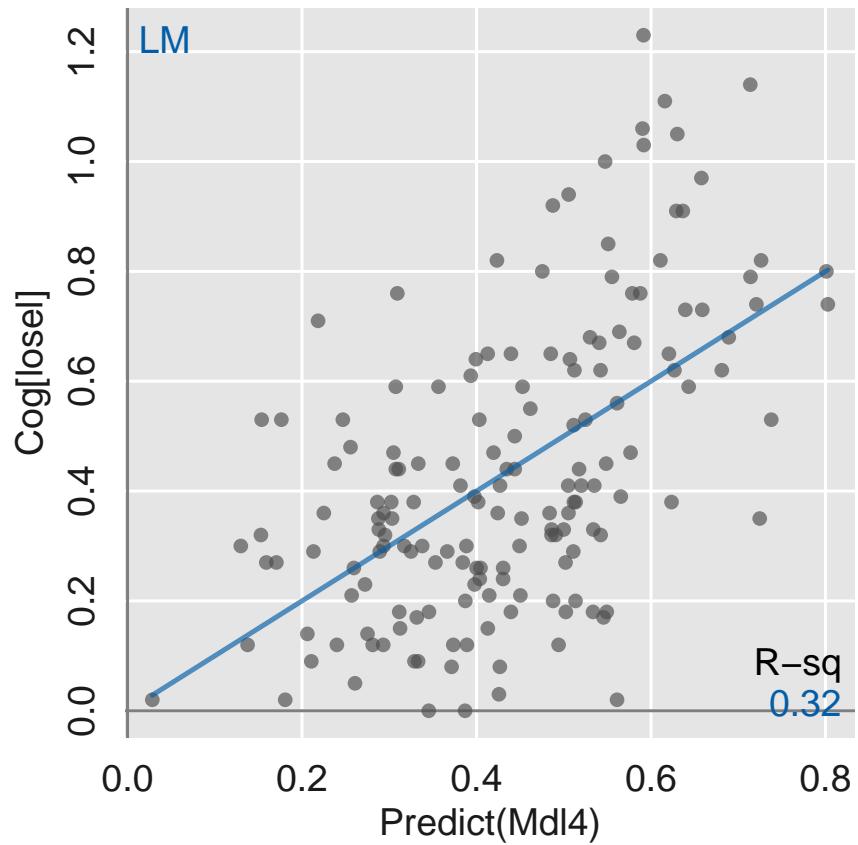


Figure 3: SyMILR Anxiety

symilr prediction, for comparison:

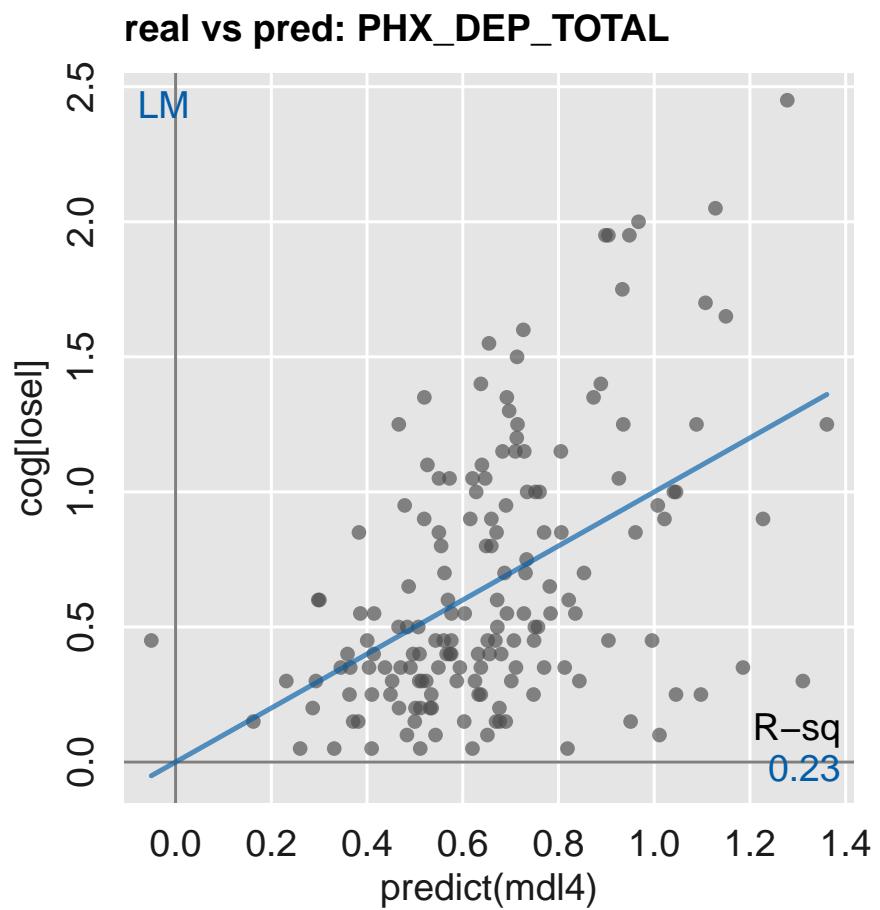


Figure 4: SVD Depression

SVD-based prediction of depression

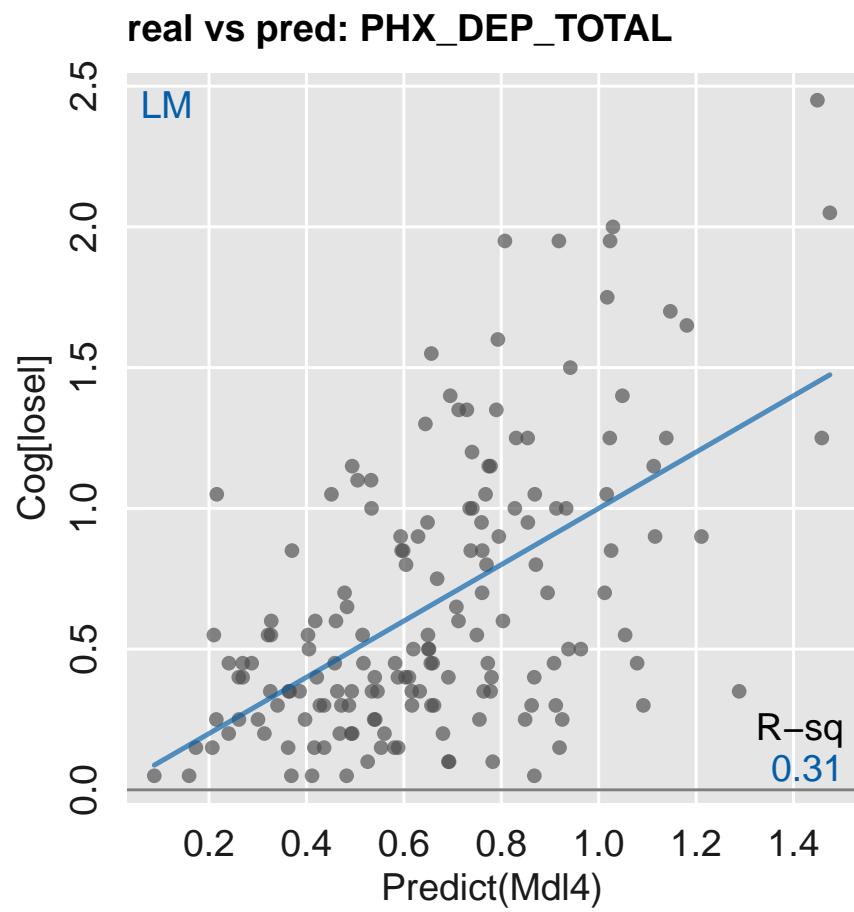


Figure 5: SyMILR Depression

symilr prediction, for comparison:

## **SyMILR results using pure train/test split in data *without* any clinical scores.**

Prediction of MRI-based anatomical measurements from SNPs guided parameter setting in the main paper. The resulting embeddings were tested for relationships with clinical anxiety and depression measurements. Although no use of clinical measurements was made during parameter setting, the reviewer requested a second analysis that did not reference any MRI data from the population that contained clinical measurements. The results, are, overall similar in this second set of analyses to that provided in the main paper. The figures are below. Model R<sup>2</sup> for depression is 0.26 and for anxiety is 0.31.

### real vs pred: PHX\_ANX\_TOTAL

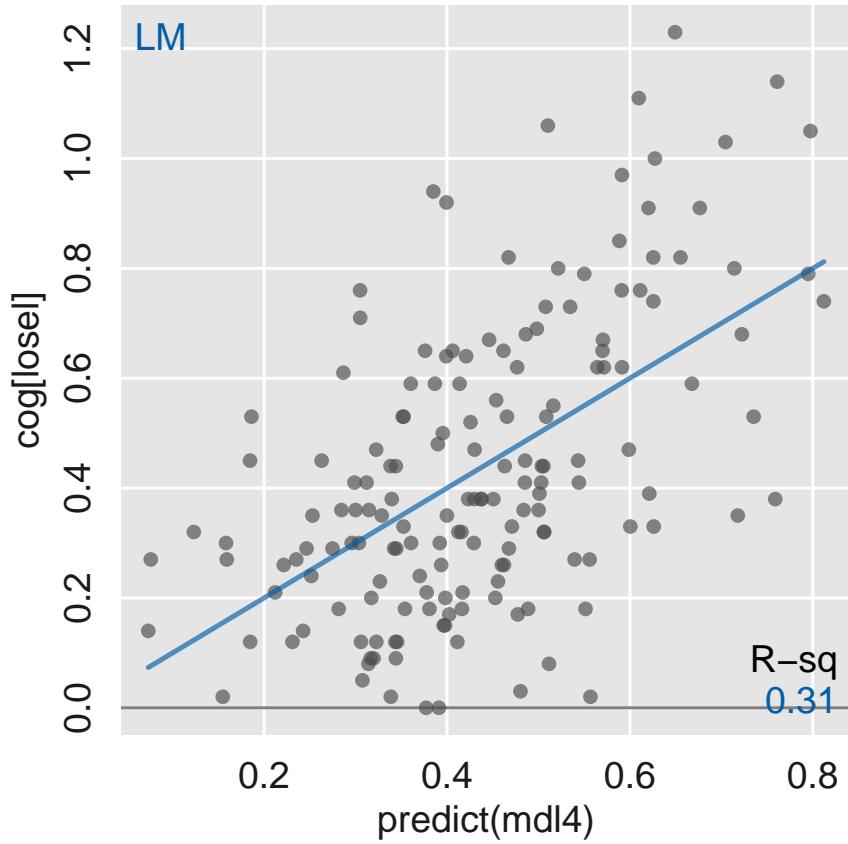


Figure 6: SyMILR Anxiety

Supplementary SyMILR-based prediction of anxiety

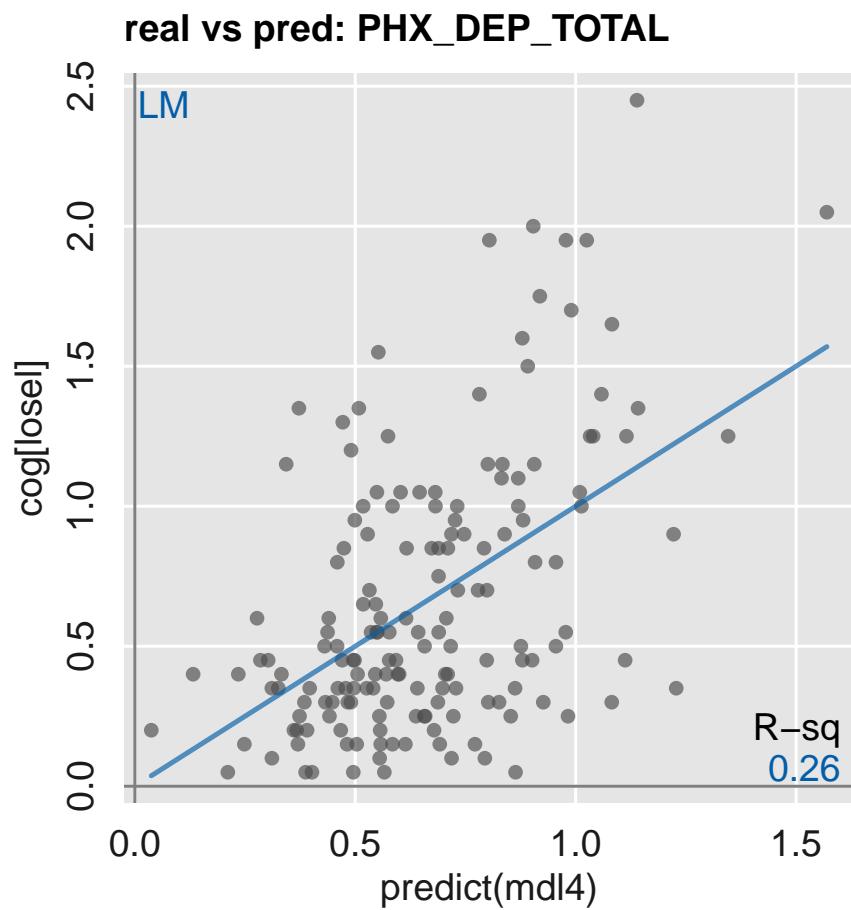


Figure 7: SyMILR Depression

Supplementary SyMILR-based prediction of depression

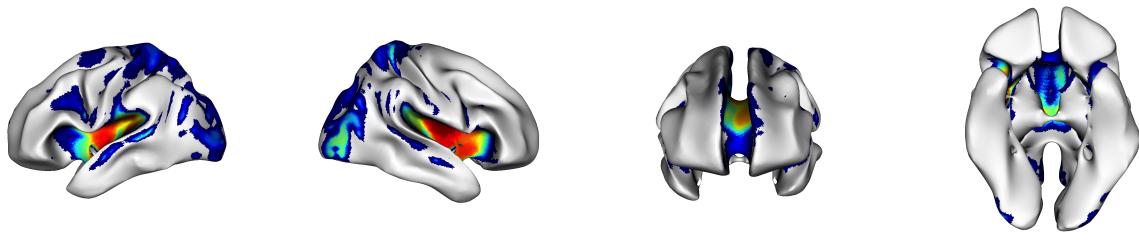


Figure 8: Thickness

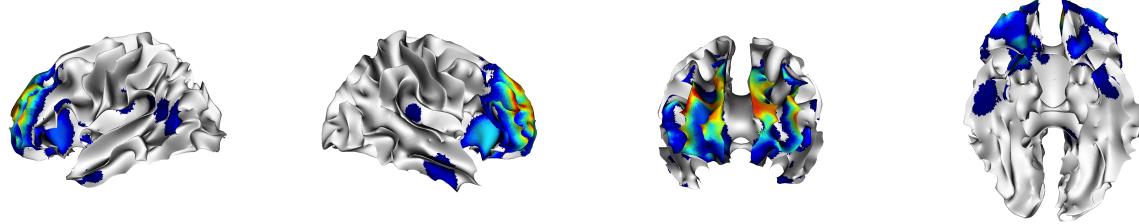


Figure 9: FA

## Supplementary visualization of embeddings

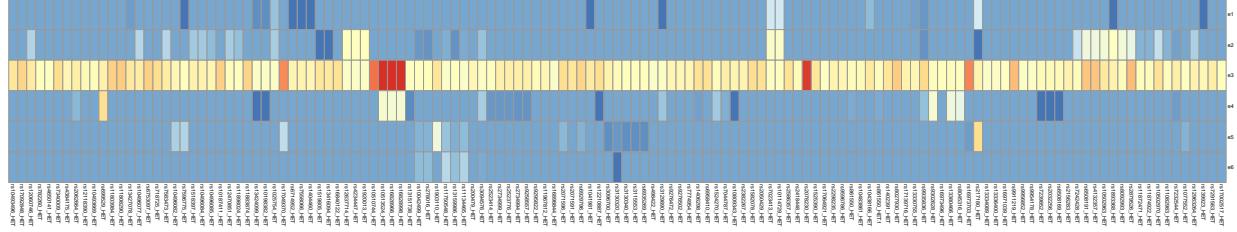


Figure 10: SNPs

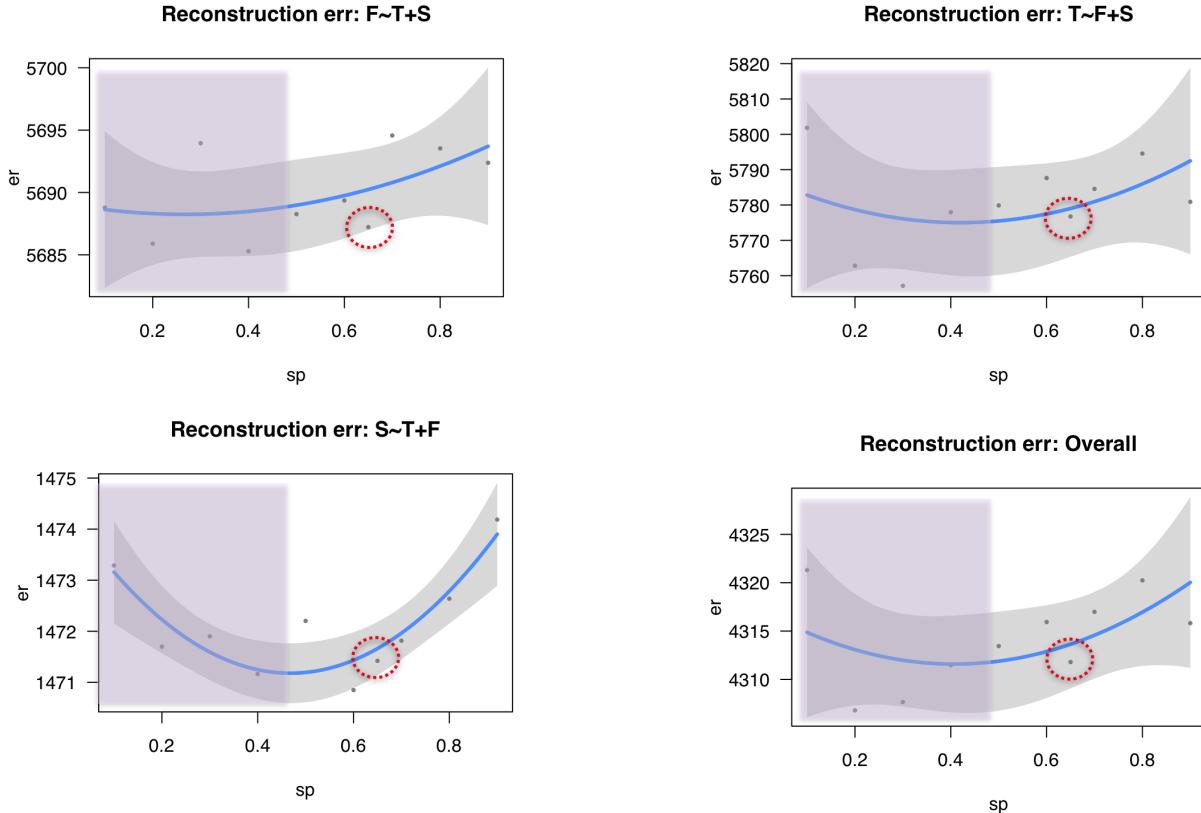


Figure 11: Reconstruction

### Selecting an operating point based on reconstruction

We evaluate reconstruction error in test data to determine a “best” sparseness parameter value for the SNP data. Prior selected values were used for neuroanatomical data. The shaded area was not searched but is shown here for completeness. It was not searched because we restricted the parameter domain to sparseness values  $\geq 0.5$ . The selected operating point is circled. The x-axis shows sparseness values while the vertical axes are reconstruction errors.