Reviewer's report

Title: Sparse Learning and Stability Selection for Predicting MCI to AD Conversion Using Baseline ADNI Data

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Reviewer: Joshua Grill

Reviewer's report:

Dr. Ye and colleagues have added to the growing and important literature using the ADNI dataset to examine possible predictors of conversion to AD dementia from the MCI construct. The authors examine a wide range of baseline factors including demographic, genetic, and clinical variables and volumetric imaging and CSF biomarkers, as well as combinations of these variables for accuracy in predicting conversion from MCI to AD. To perform their comparisons, the authors utilize sparse logistic regression to select variable combinations and support vector machine classifiers to produce areas under the curve (AUC) as measures of predictive accuracy.

The authors find that optimal predictive sensitivity is provided by a 15-item signature that includes components of the ADAS-cog, other cognitive tests, and specific brain structure volumes. They refer to this combination as "Biosignature-15."

Major Revisions:

1. The authors do not compare the various outcomes (AUC) statistically, but frequently do suggest inferiority or superiority of various combinations. For example, is the higher AUC for the Biosignature-15 significantly greater than the AUCs of the individual components that make it up? They also state that the addition of CSF "did not perform as well as Biosignature-15." It is unlikely that this combination was statistically poorer. This must be addressed in the reporting of their findings, either by performing statistical comparisons or carefully describing the results and including a discussion of the lack of statistical tests.

2. Similarly, in Figure 3, the authors suggest that for 13-15 selected features there is a stabilization of AUC scores. How was this decided, simply by visual inspection? Is there a difference between 10 and 13 variables, 9 and 12, 8 and 11?

3. The authors fail to recognize the limitations of their study. These include those stated above, as well as the fact that ADNI is a single homogenous sample of highly educated and motivated volunteers.

Minor Revisions:

1. The abstract needs to be restructured so that the included text fits the headlines (i.e. add a methods section, only include results in the "results" section)
Discretionary Revisions:
1. Table 3 is referenced before Table 2.
2. The last sentence in the Discussion states that the current results are consistent with the sensitivity of CSF measures as predictive of MCI in normal cognition. The current results do not address the transition from normal to abnormal cognition.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests