

## Reviewer Report

**Title: A highly predictive signature of cognition and brain atrophy for progression to Alzheimer's dementia**

**Version: Original Submission**    **Date: 11/17/2018**

**Reviewer name: Yu-Dong Zhang**

### Reviewer Comments to Author:

A multimodal signature of Alzheimer's dementia was first extracted using machine learning tools in the ADNI1 sample, and was comprised of cognitive deficits across multiple domains as well as atrophy in temporal, parietal and occipital regions. The authors then validated the predictive value of this signature on two MCI cohorts.

(1) How do you select the baseline of T1 scans of ADNI?

(2) What preprocessing techniques did you use? Did you perform any normalization technique?

(3) Why use GMV and TIV?

(4) Is your method a type of VBM technique?

(5) Line 168, why use a linear support vector machine (SVM)? Did you consider to use kernel SVMs?

(6) Some AD detection methods could be discussed, see "Multivariate approach for Alzheimer's disease detection using stationary wavelet entropy and predator-prey particle swarm optimization" and "Single Slice based Detection for Alzheimer's disease via wavelet entropy and multilayer perceptron trained by biogeography-based optimization"

(7) How do you optimize the hyperparameters of SVM?

(8) What type of t-test did you use? How did you set the confidence threshold? Did you use ANOVA?

(9) How do you combine and generate the final signature?

### Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

### Conclusions

Are the conclusions adequately supported by the data shown? Choose an item.

### Reporting Standards

Does the manuscript adhere to the journal's guidelines on [minimum standards of reporting?](#) Choose an item.

Choose an item.

### Statistics

Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Choose an item.

### **Quality of Written English**

Please indicate the quality of language in the manuscript: Choose an item.

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