Reviewer’s report

Title: Pattern of neural responses to verbal fluency shows diagnostic specificity for schizophrenia and bipolar disorder

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Reviewer: Stephen Lawrie

Reviewer’s report:

Costafreda et al. use machine learning to discriminate between schizophrenia and bipolar disorder and healthy controls using verbal fluency fMRI data. Altered function in plausible brain networks achieved high (80-90%) group discrimination. The manuscript is well written and the scientific message clear.

I only have minor essential revisions:

In the results section, the machine learning classification analysis sensitivity and specificity figures are given but these presumably can be increased or decreased by altering settings during the machine learning. In other words, is the machine learning classification generally taken to optimally balance sensitivity and specificity, or is it prioritising one over the other? Please comment in the methods, results or discussion.

The authors discuss the importance of current and previous psychotic symptoms in the bipolar group but as far as I can see have not mentioned how many of their subjects have suffered from psychotic symptoms in the past.

The main limitation of this paper and indeed the field as a whole is the lack of an independent test set of patients to evaluate the machine learning parameters in another group. This should be acknowledged.

The discussion mentions that this is an unusual sample, being comprised of approximately 50% twins. This might reduce variance within each of the groups and thereby increase separation between diagnoses artificially. The other difference between the groups which should also be acknowledged is that the bipolar disorder group are approximately 6 years older on average than either of the other 2 groups, which again might have been expected to facilitate the differentiation.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests