Reviewer's report

**Title:** Systematic Review of Genome-wide Gene Expression Studies of Bipolar Disorder

**Version:** 1  **Date:** 12 June 2013

**Reviewer:** Matthew Hill

**Reviewer's report:**

Seifuddin et al report results of a systematic mega-analysis of bipolar disorder brain gene expression studies. They apply a rigorous analysis pipeline in an attempt to control for confounding factors and potential sources of bias. The manuscript is well written and clear.

I have several comments:

1. The authors mention several notable genes in the results section and discussion e.g DUSP6, CRH, NPY. However, the associated p-values etc are only present in the additional files. It would be appropriate to present these in the results/as a table. Also, the authors refer these as candidate genes for mood disorders but do not included references. These should be added.

**Major Compulsory Revisions**

2. The methods section does not included sufficient detail on the pathway analysis using DAVID. For example, what background gene set was used? The most appropriate would be all detected probes for each analysis. What terms were included e.g. biological process, molecular function, KEGG etc?

3. The authors discuss a single gene category, metallothionein and metal-ion binding proteins, identified by DAVID but do not report a specific FDR for this term. Indeed, it would be beneficial to include a results table with all terms identified with a FDR<0.05.

4. The authors discuss neuropeptide genes after reporting results from the DAVID analysis, but it is not clear if these belong to a significant category or are author derived observations. The distinction between any formal testing of gene sets e.g. using DAVID and author observations needs to be made clear. The choice to discuss several of these genes e.g. NPY and SST may not be justified if additional gene sets have been identified by formal analysis. (see 4).

**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.