Reviewer's report

Title: Psychosis candidate genes in the prefrontal cortex: Meta-analysis of gene expression microarray studies

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Reviewer: Albert Wong

Reviewer's report:

The authors describe in a clear and concise way their meta-analysis of gene expression microarray data, comparing subjects with and without psychotic symptoms. A dimensional rather than categorical organization of behavioural syndromes may correspond more closely to the neurobiology underlying psychotic symptoms, so their approach is warranted. These investigators are well-positioned in their role at the SMRI to conduct this study, and they find robust changes in gene expression associated with psychosis. The main findings are upregulated metallothionein genes in psychosis, which has been reported in only one previous paper, and decreased expression of neuropeptide RNAs, for which there have been earlier reports.

Overall, the results point to a novel set of candidate molecules that may be important in the neurobiology of psychosis. How this fits with the existing genetic and gene expression data implicating strong etiological candidate genes in schizophrenia remains unclear, and so further work is required to understand the mechanisms that connect metallothionein and neuropeptide function to that of genes like NRG1, DISC1 and DOAO, as well as neurotransmitter systems involved in psychosis such as dopamine, glutamate and GABA. Overall, I feel this paper is an important contribution to the literature, and will be of interest to those in the field.

A few minor comments:

Page 20: “… NR4A2 knock-out mice suggested that these animals showed psychotic symptoms” To be precise, it would be better to state that these animals showed behaviours related to psychosis in humans or that behavioural endophenotypes resembled that seen in other animal models of psychosis/schizophrenia. Obviously one cannot assess core psychotic symptoms directly in any animal.

Page 21: “Psychotic feature is an overlapping …” should be “Psychosis is an overlapping …”

Page 15: “Most of individual studies show …” - delete “of”

Level of interest: An article of importance in its field

Quality of written English: Acceptable
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