Reviewer's report

Title: Model-based parametric study of the frontostriatal abnormality in schizophrenia patients

Version: 1 Date: 24 June 2009

Reviewer: W. Gordon Frankle

Reviewer's report:

This is an interesting modeling paper which uses receptor imaging data to model the effects of hypofunction of the prefrontal cortex on subcortical dopamine levels in schizophrenia. While at times the mathematical modeling was difficult to follow for someone without the background in this field the author nicely summarizes the findings of the paper.

A few discretionary revisions may help to enhance the clinical relevance of the paper. First, the author may want to comment as to which studies should be performed to test his model - would these be PET receptor imaging studies, fMRI studies, or a combination of these. It would be nice to see the predicted outcomes of the recommended studies based on this model; that way, in the future, if these studies are performed, the model would be tested.

Also, while the author does comment briefly on the effects of antipsychotic medications as they relate to the PFC, it would be interesting for him to discuss what effect reduced dopamine occupancy at the D2 receptor would have in the proposed model. See Frankle et al, Psychopharmacology 2004, for an estimation of the level of D2 occupancy by dopamine at different doses of antipsychotic medications - would there be an “optimum” occupancy of the D2 receptor which would maximize the PFC activity while improving the psychotic symptoms?

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