Reviewer’s report

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

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Reviewer: Albert Adell

Reviewer’s report:

This paper describes a mathematical model of so-called hypofrontality in schizophrenia. While this model offers some attractive new data, further research and a more exhaustive discussion is needed to warrant validation.

1. The concept of hypofrontality stems from the finding that malfunction of NMDA receptors leads to the development of schizophrenia-like symptoms. However, this effect ultimately causes an excessive release of glutamate (hyperglutamatergia) in cortical regions. For this reason, the term hypofrontality needs a clear definition in this context.

2. This is further complicated by the fact that hypofrontality has been generally associated with negative (but not positive) symptoms of schizophrenia. The author fails to provide relevant literature in this respect (Wolkin et al., Arch Gen Psychiatry 1992; Whalley et al., J Affect Disord 2008; Park et al., Psychiatry Res 2009).

3. Given that the author does not measure the reduction of endogenous dopamine after AMPT (p. 5), a reference must be provided.

4. The manuscript would definitely benefit from some artwork depicting the circuit model described in the section 2.1.

5. Overall, the discussion fails to confront the model described with relevant clinical (and preclinical) data existing in the literature. It is surprising that only two references are provided. The discussion section is usually conceived as a justification of present data as well as a comparison of previous findings. This important action is missing in the present paper.

Level of interest: An article of limited interest

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