Author's response to reviews

Title: Metabotropic glutamate receptor 5: a candidate in psychiatric pathology? Implications for novel mGluR5-based therapeutics

Authors:

Kelly A Newell (knewell@uow.edu.au)
Natalie Matosin (nj307@uowmail.edu.au)

Version: 2 Date: 31 December 2013

Author's response to reviews: see over
Dr Joshua Kantrowitz  
Associate Editor,  
BMC Psychiatry  

Re MS: 1099104478109564  

Dear Dr Kantrowitz,

Thank you for the comments on our paper titled “Metabotropic glutamate receptor 5: a candidate in psychiatric pathology? Implications for novel mGluR5-based therapeutics”. We are grateful for all comments and suggestions made by the reviewers.

We have thoroughly addressed all comments made by the reviewers. Please find the response to reviewers’ comments enclosed.

Thank you for considering our manuscript for publication in BMC Psychiatry.

Yours sincerely,

Kelly A. Newell, PhD
Response to Reviewers

Reviewer 1

Q1. This article would be greatly improved by greater streamlining and structure. There is a review of the neuropath literature, as well as brief discussions about associated structures/proteins, procedural limitations of the neuropath literature, comparisons with MDD, discussions about regional and neuronal population variability in mGluR5 findings, and a discussion about NAMs and PAMS. These components all seem to be important, but are presented in a somewhat disorganized manner that takes away from the message of the paper. In addition, the manuscript seems to switch from depression to schizophrenia too readily. It might also be helpful to first discuss the results from the literature for both diseases separately, and then present a larger synthesis section where the findings are interpreted and critically discussed, since it seems that there are numerous issues in the literature that are common to both. Subheadings would be an additional means by which to add greater organization to the paper.

A1. The paper has been reorganised to allow more clarity. In addition, subheadings have now been added to the main discussion, allowing greater organisation of the paper.

Q2. While the focus in the paper is rightly on the mGluR 5, it is difficult for the reader to understand why the mGluR 5 is relevant (i.e., why a NAM in MDD and a PAM in schizophrenia) without a discussion of the relationship between the mGluR 5 and the NMDAR, and without presenting the basic NMDA based hypotheses in MDD and schizophrenia.

A2. The authors have added the relevant information to the “Background” section of the paper discussing the interaction between NMDAR and mGluR5 and the relevance to schizophrenia and depression (page 4, paragraph 1 and 2).

Reviewer 2

Q1. Add a paragraph on pharmacological trials on the effect of mGluR5 ligands in animal models of schizophrenia and major depression.

A1. A paragraph has been added to the “Discussion” section of the paper (page 10, paragraph 2).

Q2. To add a short paragraph on the possible role of mGluR5 in anxiety disorders and autism spectrum disorders, at least at the level of animal models and pre-clinical data.

A2. A short paragraph has been added at the end of the “Discussion” section of the paper (page 11, paragraph 2).

Q3. The authors could use the review by Krivoy A, Fischel T, Weizman A. The possible involvement of metabotropic glutamate receptors in schizophrenia. Eur Neuropsychopharmacol. 2008;18:395-405, to show the interaction between the mGlu receptors and their relevance to psychopathology.

A3. The authors have now referenced this review (page 4, paragraph 1).