Reviewer's report

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

**Version:** 1  
**Date:** 24 November 2013

**Reviewer:** Ragy Girgis

**Reviewer's report:**

Newell and Matosin have written a review paper on the type 5 metabotropic glutamate receptor, with a focus on the neuropathology of the receptor, and neuropathological implications for drug development. Overall, this was an interesting article, with information that is useful for individuals with an interest in understanding the relatively negative neuropathological studies of the mGluR 5 in schizophrenia. In addition, the language and grammar of this article were excellent.

There are two primary suggestions that this reviewer believes would strengthen the paper (major compulsory revisions).

1) 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 mGluR 5 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.

2) 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.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have received research funding from Otsuka.