April 24, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: _____.doc). We have also included a copy of the manuscript with tracked changes
(file name: SynIIReview(04.24.15).docx).

Title: Role of presynaptic phosphoprotein synapsin II in schizophrenia
Authors: Luke Molinaro, Patricia Hui, Mattea Tan, Ram K. Mishra
Name of Journal: *World Journal of Psychiatry*
EPSP Manuscript NO: 16984

The manuscript has been improved according to the suggestions of the esteemed editor and reviewer:

1. In response to: *Abstract section does not cover data on clinical signs of schizophrenia. This section should cover important effect of clinical and pathophysiology of synapsin II on the schizophrenia.*
   We thank the reviewer for the thorough comments and we agree that there is a limited amount of clinical data presented in the abstract. We have now added to our abstract, a more comprehensive background regarding the clinical implications of synapsin II in schizophrenia. We have also provided an in-depth comprehensive review of the clinical impact of synapsin II within the clinical population within the section "Implications of Synapsin II in Schizophrenia." Furthermore, we elaborated the effect of antipsychotic drugs on expression levels of synapsin II in the clinical population in the section "Neurocircuitry, Antipsychotic Drugs and Synapsin II" of the review paper.

2. In response to: *...there is insufficient data in this study showing the particular importance of clinical aspect of synapsin II.*
   We appreciate the reviewer's comments about not having enough discussion on the clinical importance of synapsin II in schizophrenia. There are innate challenges in the execution of clinical studies, and proving direct causation can be a challenge given inter-subject variability.
   Although it is difficult to fully implicate synapsin II with schizophrenia, findings from clinical genome-wide scans and post-mortem studies *strongly* suggest a role for synapsin II in the pathophysiology of schizophrenia. These clinical findings were further supported by specific gene manipulation in preclinical studies from our laboratory. Furthermore, we present evidence that current therapeutic approaches at mitigating symptoms of schizophrenia were found to effective at normalizing altered synapsin II levels. These

findings from these studies are discussed in greater detail in the manuscript under the heading, "Implications of Synapsin II in Schizophrenia," toward the end of page 7.

3. The following sections have been added to the manuscript:
    a. Running title
    b. Key words
    c. Core tip & audio core tip (see attached file: SynII_CoreTip.wav)

4. Formatting and typesetting of the manuscript, figures, and references have been adjusted to match the journal's requirements.

Thank you again for accepting and publishing our manuscript in the *World Journal of Psychiatry*.

Sincerely,
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