Format for ANSWERING REVIEWERS

June 23, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 18274-Review.doc).

Title: Risk for emerging bipolar disorder, variants, and symptoms in children with attention deficit hyperactivity disorder, now grown up

Author: Ahmed Z Elmaadawi, Peter S Jensen, L Eugene Arnold, Brooke SG Molina, Karen Wells, Lily Hechtman, Howard B Abikoff, Stephen P Hinshaw, Jeffrey H Newcorn, Laurence Lee Greenhill, James M Swanson, Cathryn Galanter

Name of Journal: *World Journal of Psychiatry*

ESPS Manuscript NO: 18274

Thank you so much for your thoughtful and detailed review of our research article. Following your recommendations, and suggestions, the following changes were made to the article:

1. Reviewer # 2156774:

a. *Methods: A. How was the reliability of these measurements?* Reliability of DISC as an NIMH established tool for the diagnosis of over 30 different psychiatric diseases. The background of DISC was added to the method section along with appropriate references.

b. *Results: A. Please show the demographics of the two groups (age, gender, etc.).* Demographic information was added.

c. *Table 1a: Please fill values of the two cells (n/N=0% and n/N=0.41%) in the right column disease DISC.* Info was added to the table 1a

d. *The results of Bipolar Symptom Level and Table 2: Due to there was significant change of symptoms in groups over time, it would be better to revise the statement of "Thus, …… they did have almost twice the rates of bipolar-mania symptoms at the 4 assessment points, and over time." (P.9)* Statement was revised.

e. *The bottom line of Table 2 was not clear. D. There is a typing error of 'F194.7' (P.9).* Error was corrected.

f. *Figure 1 & 2: It needs to show the points of the different groups in the scatter plots. Provide the time*

unit of the horizontal axis. Information was corrected.

g. *Discussion: A. The authors mentioned 'These findings raise questions about the stability of BD diagnoses over time, especially during early development --assuming reliability of the DISC, DIS, and DISC-YA' in the first paragraph. So, the reliability of those measurements is* The limitation of reliability of DISC was discussed in the method section and end of discussion as one of the study limitations *important issues and needs to do more discussion, and also their limitations.*

h. *B. The rationale about TSC analyze should be mentioned in the previous. What dose TSC scores means? It might be just some behaviors looks as. Could this be an indicator of BD severity or just the amount of BD symptoms which subjects could perceive? Besides, it might be easier for clinicians than subjects, to differentiate NSM symptoms from ADHD symptoms.* TSC stands for total symptoms count. DISC Mania module has a complex set of questions that cover each bipolar manic symptom. Each symptom does not count as positive unless it fulfills rigid criteria satisfying the duration, the severity, and impairment in function. For example; the symptom of "decrease need for sleep": if patient answered yes to the general question, then there are additional questions which will be asked by the interviewer inquiring about duration of the symptom, other people noticing the symptom, and if there has been any change in function. If answers are yes for all questions, then the patient will be scored as "yes" for decrease need of sleep. This insures more accurate findings to identify the bipolar symptom. Bipolar severity was not studied based on how high the TSC score is for each patient, since it is considered more of a clinical judgment. It is highly possible that a higher TSC score will predict severe Bipolar disorder.

2. Reviewer # 02445209:
I do not have any negative comments on your manuscript. Best regards
Thank you

3. Reviewer # 02445261
   a. *Generally, I believe that the Introduction section is too long and needs to be reduced in length; it seems that some parts of the manuscript, as presented, may be more appropriately inserted throughout the Discussion section.* In the introduction section we thought of presenting one of the most debatable topics in the field of child psychiatry that usually leads to heated discussions in national meetings. The general reader may need to learn about the background and different efforts that led to this paper. Also, our study yields several results with many different correlations. We did not want to lengthen the discussion section or distract the reader, especially with many abbreviations

   b. *Furthermore, throughout the same section the authors frequently used many abbreviations (e.g., BP-NOS, ADHD, comorbid with ODD, etc.) without appropriately specifying them extensively. This results quite unclear for the general readership.* Abbreviations were revised and explained more in the introduction and method section.

   c. *Within the Methods section, whether the local review board approved the study design and whether parents of the 579 recruited children have signed a regular informed consent have not been reported.* Information was added to the method section.

d. *Moreover, exclusion criteria need to be more carefully specified.* Information was added to the method section. There were no specific exclusion criteria, other than the original MTA study design as required.

e. *Interestingly, according to the authors' point of view the present findings raise questions about the stability of BD diagnoses over time, in particular during early development. However, it is also important to state (as correctly reported by the authors throughout the limitations section) that the authors adopted in their study a structure interview (DISC) that does not consider invalid responses or atypical presentations. Therefore this may explain why subjects with childhood ADHD followed into early adulthood (ages 21-24) do not appear to be at a significantly greater risk for developing the full diagnostic picture of BD than comparison subjects. I believe that this last observation may be more carefully reported by the authors throughout their Discussion section.* Discussion was revised to discuss DISC limitations.