

November 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (Revision_MS 14351_Final.docx).

Title: Smoking in Schizophrenic Patients: A Critique of the Self-Medication Hypothesis

Author: Francesca Manzella, Susan E. Maloney, George T. Taylor

Name of Journal: *World Journal of Psychiatry*

ESPS Manuscript NO: 14351

Comments for Editor:

Please note that order of the authors has been changed. Given the extensive revision of the original manuscript, Dr. Maloney and I agreed that Ms. Manzella deserves the 1st author position. Also, sections of the MS that have been significantly revised have been highlighted in yellow.
G. Taylor

The manuscript has been improved according to the suggestions of reviewers:

1. Revision has been made according to the suggestions of the reviewer.

Reviewer 1.

(1) A paragraph has been added on the relation of cannabis smoking schizophrenia (p. 25)

(2) We also have been careful to acknowledge the difficulty with making a prediction about ages of onset of smoking and a schizophrenia diagnosis (p. 16-21). Indeed, we admit that it really is a judgment call but concluded in our summary for that section that 4-5 yrs differential is enough to convince us that it is unlikely that there were obvious symptoms that long ago (p. 18).

(3) We have added the reference to smoking activating the P450 hepatic enzymatic, thus reducing circulating levels of antipsychotic drugs (p. 24)

(4) Grammatical and punctuation errors have been corrected.

There are multiple places where there are issues with grammar and punctuation. I would recommend a careful perusal to polish it into a publishable format. Some examples: -

In the abstract 1980's should be 1980s -

In the second paragraph of the Introduction (page 5), the last sentence and punctuation do not make sense. -

On page 14, the first sentence of the paragraph that starts with "Also, studies of smoking..." does not make sense. -

On page 15, the beginning of the third paragraph should be changed from "In another, recent report, " to "In another recent report, ". -

On page 16, the first sentence of the third paragraph should be changed from "Studies of the sexual behavior" to "Studies of sexual behavior". A reference should be added at the end of that sentence. –

On page 22, in the first paragraph of the Summary and end of that sentence.

On page 22, in the first paragraph of the Summary and Conclusions, "schizophrenia" should be changed to "schizophrenia".

Reviewer 2.

(1) We have added the suggestion to discuss the mechanism for the reinforcing and dependency effects is the interaction of nicotine with the VTA (p. 11)

(2) We have corrected the pathways responsible negative and positive symptomology (thank you for catching that embarrassing error).

(3) All words requiring hyphenations have been corrected.

Reviewer 3.

(1) Predictions with multiple components have been separated so that the prediction list has expanded from 5 to 8, along with discussions of each.

(2) As you can see from extent of the highlights of new or changed sections, we have worked very hard to satisfy Reviewer 3.

(3) Included are clearer presentation of the logic of the predictions and the relation of the studies reviewed. Moreover, we have made it clear that there are other predictions not included here (p. 11 and again on p. 32). We only hope that others will take our lead to expand critical reviews of controversial topics in psychiatry.

(4) We also want to thank Reviewer 3. It is a better paper because of the rather severe criticisms of the Reviewer. It forced us to rethink multiple issues.

2. General formatting has been corrected as well as references

Again, thank you for reviewing our manuscript for *World Journal of Psychiatry*.

Sincerely yours,

A handwritten signature in cursive script, reading "Susan E. Maloney". The signature is written in dark ink on a light background.

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