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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Psychiatry

ESPS manuscript NO: 14351

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

Reviewer code: 02445381

Science editor: Xue-Mei Gong

Date sent for review: 2014-09-29 15:55

Date reviewed: 2014-10-10 03:34

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is a thoughtful and well-articulated manuscript on the self-medication hypothesis (SMH) as it relates to smoking. The authors present their hypotheses based on the current literature and have a balanced discussion of the theories. When it comes to SMH in schizophrenia, another drug that is often discussed is cannabis. It would be helpful for the authors to include a brief paragraph on how the SMH as it relates to smoking relates to the SMH as it relates to cannabis. On the topic of prediction C, the authors state that the data is not consistent with the prediction because smoking often precedes the first psychotic break. We need to add a note of caution here since the subtle psychopathology of the prodromal phase precedes the first psychotic break by a few years and is accompanied by symptomatology such as difficulties with attention, increased anxiety etc. So, patients starting to smoke a year or two before the first psychotic break would arguably still be consistent with prediction C. This would be true for cannabis as well, where the use/abuse starts during the prodromal phase preceding the psychotic break. In the section on SMH as a way to alleviate side effects of medications, it would be interesting to see if there is any literature specifically focusing on akathisia related to antipsychotic medication and smoking appears to relieve that. The other issue to take into account is also the effect of smoking on the cytochrome P450 system. Smoking is known to induce CYP1A2, whose major metabolites include antipsychotics such as clozapine, olanzapine and haloperidol. Based on this knowledge, smokers would metabolize the antipsychotics more rapidly and effectively than non-smokers. It is unclear how that would affect the patients but may



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help with lowering side effects by clearing the drugs rapidly or potentially metabolizing the medications faster to active metabolites, such as N-desmethyl clozapine in the case of clozapine. While the paper is well written, 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 Conclusions, "schizophrenia" should be changed to "schizophrenia".



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Psychiatry

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Reviewer code: 00646580

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<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input checked="" type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In Smoking in Schizophrenic Patients: A Critique of the Self-Medication Hypothesis, authors review the idea of smoking nicotine as a type of self-medication for schizophrenic patients. What seems to be an interesting review in the 2 first pages become something difficult to follow from a scientific and logic point of view. The predictions on table 1 are not really well articulated neither they are hypothesis, as some of them contain several hypotheses rather than one grouped in each of these predictions. I did not see the logic for formulating these particular predictions and not other and seems not to be accurate from a scientific point of view either. Moreover, when analyzed along the manuscript, these predictions are mixed so explanation for one of these predictions sometimes appear on a different section (i.e. rationale for prediction B part 2 appear on the section for prediction D). In summary, I don't think this manuscript reach standards for publication on World Journal of Psychiatry.



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Psychiatry

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Reviewer code: 00504526

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
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<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript by Maloney et al. titled "Smoking in Schizophrenic Patients: A Critique of the Self-Medication Hypothesis" is aimed to review the relationship between smoking and schizophrenia. The authors have taken into consideration the latest advances in the field. Overall the review is well written, but there are some minor points that I would like to submit to the attention of the authors to improve the scientific quality of the review.

1. page 8: It has previously been shown that the reinforcing and dependence-producing properties of nicotine depend to a great extent on activation of nicotinic receptors within the ventral tegmental area (VTA). Please discuss.
2. Page 10, lines 4-6: Please correct "A revision of the DA model concluded the positive symptoms are from prefrontal hypoactivity and the negative symptoms from striatal hyperactivity" with "A revision of the DA model concluded the negative symptoms are from prefrontal hypoactivity and the positive symptoms from striatal hyperactivity"
3. Please separate and hyphenate the words correctly.