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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16570

Title: Gluten related disorders: towards a better understanding of non-celiac gluten sensitivity

Reviewer's code: 00008517

Reviewer's country: Italy

Science editor: Ya-Juan Ma

Date sent for review: 2015-01-23 15:02

Date reviewed: 2015-02-02 19:41

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

a nice, timely, and condiced manuscript reviewing the hot topic of non-celiac gluten sensitivity. I do not have major criticisms concerning the ms; however, the authors should describe a little more in-depth the possible histological findings of NCGS, focusing on the differences (if any) with celiac disease. Moreover, the authors could recognize that, by a histological point of view, this entity could be included in those encompassing the so-called microscopic enteritis. Some histological representative pictures are needed to stress the above points.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16570

Title: Gluten related disorders: towards a better understanding of non-celiac gluten sensitivity

Reviewer's code: 00039328

Reviewer's country: United States

Science editor: Ya-Juan Ma

Date sent for review: 2015-01-23 15:02

Date reviewed: 2015-02-11 06:51

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is review on a very hot topic, and it would certainly be of interest to the reader. This reviewer has the following comments: Major criticisms. I. There is absolutely no mention in the whole paper of the possible role of FODMAP sensitivity. As the authors certainly know, the paper by Biesiekierski et al published in August 2013 represented a real paradigm shift in our thinking about NCGS, and one cannot avoid dealing with its conclusions. Thus, a proper acknowledgment and evaluation of that study in the context of NCGS is paramount and must be included. II. The statement about prevalence "Gluten-related disorders.... prevalence, increasing in the recent decades, ranges from 4% to 6% in Western countries" is unfounded. In fact, the authors provide no references for this, and this is not surprising, since one cannot estimate the prevalence of a disorder for which there is no accepted definition. Minor criticisms I. The phrase "Nowadays CD is considered an autoimmune disorder affecting about 1% of the worldwide population[7]" is indeed quite correct, but the quoted reference has nothing to do with it, being simply a report on the national Italian GI society. II. Likewise, the reference 9 quoted in support of the statement "Thus, it is actually recognised that



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gluten (or other wheat components) are the environmental factor globally involving from 6% to 10% of the population" is inadequate to support the statement. II. "NCGS is a clinical syndrome characterized by both intestinal and extra-intestinal symptoms, responsive to gluten withdrawal from the diet.". Actually, I am not aware that anyone has ever demonstrated that gluten withdrawal is beneficial in NCGS. It is wheat withdrawal that is beneficial. The distinction is fundamental. IV. "Among them the amylase trypsin inhibitor (ATI) in cells from CD and non-CD patients and biopsies". True, but the authors should acknowledge also that this is the single one paper ever showing ATI effect, and no subsequent confirmation has appeared. V. "NCGS is present in children". Where is the evidence? ref. 23 does not identify any child as NCGS, just as "avoiding gluten"; all the others are in adults. VI. "...while the second is the result of a study at the tertiary Center for Celiac Research, University of Maryland [6]" This is not a study, is just a verbal observation by Dr. Fasano, not supported by any peer-reviewed publication.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16570

Title: Gluten related disorders: towards a better understanding of non-celiac gluten sensitivity

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<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
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<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

GENERAL COMMENTS Elli and coworkers have looked into the interesting topic of gluten-related disorders that has recently attracted attentions of both clinicians and researchers. In this context, the editorial represents a confirmation of previous evidence. The manuscript is clearly presented, organized in a logical and easy sequence, and supported by appropriate references and specific experience of the Authors. However, there are a number of conceptual issues that need to be improved, the English language is slightly defective and a couple of Tables and/or a Figure might help the readers in following the article, thus it needs major modification.

SPECIFIC COMMENTS
Title: the title gives the reader the impression that in the manuscript there is a real and novel explanation of gluten-related disorders, whilst the authors simply support the widely accepted criteria for diagnosis and the current theories on the pathomechanisms of non-celiac gluten-sensitivity. Thus a less emphasis should be given to the title.
Discussion: ? First of all, a couple of Tables and/or a Figure possibly explaining the different clinical picture or mechanisms leading to gluten-related disorders are strictly required. ? The possibility that this condition is due



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to wheat-sensitivity instead of gluten-sensitivity should be discussed. ? A more detail is required in order to explain the putative pathomechanisms leading to this disorder, with a mention to low-fermentable, poorly-absorbed, short-chain carbohydrates and polyols (so called FODMAPs). ? A mention about some diagnostic tests, such as the search for the anti-gliadin class G antibody, the cytofluorimetric assay revealing in vitro basophil activation by food antigens, and the frequent presence of eosinophils in the intestinal mucosa biopsies should be added in the text. ? Finally, the financial incentives for companies promoting gluten-free products represent an issue that deserves some discussion. References: the following two important references should be inserted and discussed: - Biesiekirski JR, Peters SL, Newnham ED, Rosella O, Muir JG, Gibson PR. No effects of gluten in patients with self-reported non-celiac gluten sensitivity following dietary reduction of low-fermentable, poorly absorbed, short-chain carbohydrates. *Gastroenterology* 2013;145:320-328. - Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology* 2014;146:67-75. LANGUAGE EVALUATION: the English language is slightly defective, and a full revision from a mother tongue speaker is requested. In addition, there are a number of typos in the manuscript that must be corrected.