

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 15284

**Title:** Valproic acid and nonalcoholic fatty liver disease: A possible association?

**Reviewer's code:** 00352969

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2014-11-22 10:30

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" 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		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The authors have provided an interesting review of valproic acid (VPA)-related liver disease, specifically nonalcoholic fatty liver disease (NAFLD) in children in which VPA is used to treat epilepsy. They also discuss other metabolic derangements such as development of insulin resistance, dyslipidaemia, metabolic syndrome (MetS), weight gain, obesity, etc. Overall, the paper is rather well organized and written. Here are a few comments that I have on this paper: - As a pathologist, I think it would have been nice to see a histology image of fatty liver disease in a patient using VPA. Of course, I may be biased; and this may not be crucial. The editor(s) can also help gauge the degree to which this would add to the article. If the authors have worked on this in the past, perhaps one of their patients has been biopsied. The authors could involve their pathologist in obtaining an image of this biopsy and include the pathologist as a coauthor. - I was surprised that there isn't much mention of the biopsy findings in VPA therapy. Perhaps the authors could comment on this? In this regard, it may be useful for the authors to mention possible systems for judging the severity of inflammation (grading), fibrosis (staging), and steatosis in the NAFLD associated with VPA. Systems that they might want to mention include the NASH CRN and Brunt systems. In doing this,

they might want to mention the reference below with regard to the NASH CRN system that is employed in scoring NAFLD. Of course the NASH CRN system is primarily used for nonalcoholic steatohepatitis [not associated with alcohol or drugs]. o Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, Ferrell LD, Liu YC, Torbenson MS, Unalp-Arida A, Yeh M, McCullough AJ, Sanyal AJ; Nonalcoholic Steatohepatitis Clinical Research Network. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*. 2005 Jun;41(6):1313-21. PubMed PMID: 15915461. - Table 1 is a nice addition to the paper in providing a quick background to the reader of this type review article; however, it might be nice to add some measure of the frequency of these disorders in the use of VPA. It would have also been nice to see a table summarizing some of the key studies relating VPA therapy and the development of NAFLD in children. An inclusion of some statistics from the studies such as odds ratio, hazard ratio, or some other measure could be included in such a table in a meta-analysis-type approach. - Perhaps the authors could briefly discuss and cite their own work as a way of engaging the reader and providing an introduction into their expertise in this field? This probably isn't crucial, but it might be a nice addition. - Their discussion of the molecular pathways involved in VPA is complicated. Perhaps a graphic of some of the key pathways and VPA's place in all of this would be good? - On page 8 of the pdf version of the manuscript, the authors state that "...consequently cause pancreatic beta-cells dysfunction..." I think this is supposed to be "... dysfunction of pancreatic beta-cells..." For the most part though, the paper is well written; however, the authors may want to have their paper written by another native English speaker since I may have missed some things.

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**Name of journal:** World Journal of Hepatology

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<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In this manuscript, the authors review the current knowledge of the association between valproic acid use and nonalcoholic fatty liver disease. The manuscript is well written. However, it still needs some polishing in grammar. My comments are attached.