

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16019

Title: The endozepine-4 levels are increased in hepatic coma

Reviewer's code: 00032726

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2014-12-22 20:56

Date reviewed: 2015-01-06 20:02

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

Endozepine-4, an endogenous ligand for the benzodiazepine (BZ) recognition site on the γ -aminobutyric acid type A receptor (GABAAR), may play an important role in the pathogenesis of hepatic encephalopathy (HE). In this article, the authors evaluated the serum endozepine-4 levels to explore its correlation with clinical scales and plasma concentration of ammonia. They reported that endozepine-4 was markedly elevated in patients with grade IV hepatic coma and/or high scores of the Model for End-Stage Liver Disease (MELD). They also identified the significant correlation between serum endozepine-4 levels and the ammonia concentration. Generally, the outcome of this study should be helpful for clinicians to confirm the diagnosis of an advanced stage of HE and to give a comprehensive assessment of the patient. However, the manuscript was not well prepared and there are several points should be addressed before further consideration. 1. To have appropriate statistical power, the sample size should be large enough. Given the wide range of age (18-70 years) and clinical types (being classified according to cirrhosis types, Child Pugh score, MELD score, and coma grading), the sample size of this study (20 cases and 20 controls) is not large enough to ensure the power, nor to avoid bias. Since the cases of HE are scarce and controls relatively to obtain, it is

appropriate to increase the ratio of controls to cases. 2. In table 1 and 2, the authors displayed the information of “ MHE controls”. However, the term “MHE controls” was not defined in the Material & Method section, and the data was neither analyzed in the result section nor mentioned in the discussion section. 3. In table 2, there is an obvious error in the data of “Serum albumin”. Since the difference of the serum albumin levels between patients (2.78 ± 0.6) and controls (4.1 ± 0.31) was significant ($P < 0.001$), the result of the comparison between controls (4.1 ± 0.31) and MHE controls (39 ± 0.61) should not be null ($P = 0.19$). 4. The manuscript was not prepared with sufficient care. Three-line tables are required, and vertical lines should be omitted. There are two tables without any title and not numbered. Standard abbreviations should be defined in the abstract and on first mention in the text, and should be listed in the abbreviations list. Decision: Major Revision

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16019

Title: The endozepine-4 levels are increased in hepatic coma

Reviewer's code: 00002314

Reviewer's country: Italy

Science editor: Yuan Qi

Date sent for review: 2014-12-22 20:56

Date reviewed: 2015-01-04 22:40

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an interesting manuscript for both basic and clinical research. POINTS TO CONSIDER - The study enrolled 20 patients and 20 controls: however, in the methods section, only patients are mentioned. The subjects used as controls should be specifically indicated, uploading the specific consent form signed by the subject themselves (the form uploaded by the authors refers only to patients with coma, with signature by relatives) - The authors might consider providing a general overview on the role of endozepines also in other conditions, for instance by considering the following reference: Increased plasma levels of endozepines, endogenous ligands of benzodiazepine receptors, during systemic inflammation: a prospective observational study. Clavier T, et al. Crit Care. 2014;18(6):633. PMID: 25407756 - The concluding remark could probably be expressed more clearly by saying: Involvement of the GABA-ergic system in HE coma could be due to stage-specific alterations in endozepine levels. - Figure 1 can easily be omitted - The authors state that all of them "contributed equally to this work". However, in my opinion, it is more appropriate to identify and acknowledge each author's contribution separately. - Some likely typos: e.g. in the discussion: "Endozepines, peripheral BZ receptors, are located" (endozepines are ligands); NaPO4; etc. - In



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general, the manuscript needs careful style/grammar revision by a native speaker, because I noticed several typos/style issues.