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8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology
ESPS manuscript NO: 18190
Title: Current understanding of the neuropathophysiology of pain in chronic pancreatitis
Reviewer's code: 00002970
Reviewer's country: Denmark
Science editor: Fang-Fang Ji
Date sent for review: 2015-04-12 00:30
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The review is flawed by the authors not being familiar with the visceral pain system. Nevertheless they have done their best to include most relevant references on this topic and the review is of interest for the readers of the journal. However, it needs a linguistic revision and a proper study of pain neurophysiology (to be included in the revised text) before considered for publication. I have more specific comments below: Introduction: In figure 1 (and the corresponding text in the manuscript) the term "central pain sensitization" is wrong. The patients suffer from sensitization of the nervous system (peripheral or central) and this may lead to pain Neurophysiology: There is no somatic nerve innervation as pancreas is retroperitoneal (the peritoneum carries a somatic nerve innervation). Second the specificity of visceral nociceptors is disputed and most visceral afferents are polymodal that are not specialized nerve endings. Be also aware that in organs such as the pancreas and ureter the afferents convey only pain, whereas in others (oesophagus, stomach and rectum) the afferents mediate pain together with other sensations. Finally, please note that T5-T9 is not the pancreatic "viscerotome" rather T10 – and anyway visceral afferent terminate widespread at

the spinal cord which partly explain the unspecific localisation of ”true” visceral pain. The authors need more specific knowledge abut the visceral pain system and are referred to e.g., F. Cervero, “Sensory innervation of the viscera: peripheral basis of visceral pain,” Physiological Reviews, vol. 74, no. 1, pp. 95–138, 1994 & C. H. Knowles and Q. Aziz, “Basic and clinical aspects of gastrointestinal pain,” Pain, vol. 141, no. 3, pp. 191–209, 2009 & Olesen SS, Krarup AK, Brock C, Drewes AM. Gastrointestinal sensations and pain: a review on basic, experimental and clinical findings. Minerva Gastroenterologica e Dietologica 2009;55(3):301-14. Abbreviations such as AMPA and NMDA shall be explained in the text. In the “Pancreatic nociception” section the authors shall stress that the role of many of the pathways are rather of interest in acute pancreatitis and the transition to chronic disease. It is not clear how “Pancreatic nociception and sensitization” can be distinguished from “Pancreatic neuropathic remodeling-induced pain” as many of the same mediators are involved in both sensitization and neuronal damage. In the central sensitization section the authors wrote that “visceral stimulation of the rectosigmoid or somatic stimulation of muscle and bone can decrease the pain threshold or increase the areas of referred pain” – this is wrong but the sensitization caused by the chronic pancreatitis decrease the pain threshold and increase the referred pain area. Later in the EEG section the authors wrote that “electrical stimulation could induce hyperalgesia and prolong latencies”. This is not true, but hyperalgesia and prolonged latencies were seen following electrical stimulation of the oesophagus.