



ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12316

Title: Chronic pancreatitis as a model of visceral pain: A systematic mechanism-orientated approach

Reviewer code: 02927089

Science editor: Su-Xin Gou

Date sent for review: 2014-07-03 13:53

Date reviewed: 2014-07-13 17:46

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" 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

In their review "Chronic pancreatitis as a model of visceral pain: A systematic mechanism-orientated approach" Bouwense et al. aim to highlight the recent progress in understanding the central mechanisms underlying chronic pain in CP and its impact on pain management. The review is written in excellent english and the references are well chosen. However, due to several points, we can not recommend the MS for publication. Major points: - The MS is too extensive. With more than 6000 words and 44 pages the authors should avoid redundancy and should avoid to give unnecessary information. - number of references should also be reduced. Many statements are substantiated by up to 6 references. Please only give the relevant references (max. 80). Minor points: - page numbers are missing - Typo in graph "peripheral sensitization": please delete "ENREF_26". This continues through the MS.



ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12316

Title: Chronic pancreatitis as a model of visceral pain: A systematic mechanism-orientated approach

Reviewer code: 02545029

Science editor: Su-Xin Gou

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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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> 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

In their current extensive review, Bouwense et al. provide a detailed description of the key concepts related to alterations in central pain processing in visceral pain syndromes with a particular focus on chronic pancreatitis (CP). They define four key questions in a mechanism-orientated approach that allows the identification of the source of peripheral nociception, and particularly the independence of central pain processing from the peripheral noxious stimulus. They also define the criteria for the development of any pain assessment tool that shall serve to decipher altered central pain processing. The authors have hereby provided a broad overview of their substantial past and current work that have helped to elucidate several novel aspects of visceral pain. The review is written in a didactic fashion, reminiscent of a book chapter. It is certainly going to be an important contribution to the field. However, I have two major and some minor comments related to this article: Major comments: 1. The authors should aim at modifying this review to become a text that goes even more beyond a reiteration of the literature. This modification can be achieved if they applied the four key questions they posed in the Table 2 for formulating a concrete diagnostic algorithm for visceral pain. The article stems from a group with extensive expertise in this area. For exactly this reason, I would have rather expected a manuscript that makes a new proposal, i.e. a new conceptual advance. There is currently need for a novel diagnostic algorithm for visceral pain, and the group that wrote this review is the most likely group who can fulfill this need. Such an algorithm would also truly fulfill the premise



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that the reader extracts from the title of this article. Concretely, which of the described diagnostic tools, i.e. QST, EEG and fMRI should be applied in which patients in which order? Are there patients in which these tests are not applicable? Once such an algorithm is proposed for CP, can it also be extended to the study of chronic pain in other visceral disorders? 2. Page 17, paragraph 3: the authors should discuss pancreatic resections (e.g. head resections) as a powerful tool of pain relief in selected cases of CP and cite clinical trials that deal with this issue. Minor comments: 1. Abstract, page 4, line 66: please provide examples for some "other visceral pain syndromes". 2. In the discussion of pain mechanisms in CP, considering citing 1) Barreto & Saccone. *Pancreatology* 2012, and 2) Demir et al., *Langenbecks Arch Surg* 2011. 3. Page 14, line 322: A suitable tool for pain diagnostics should also document the function and changes in the peripheral nervous system.

ESPS PEER REVIEW REPORT

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ESPS manuscript NO: 12316

Title: Chronic pancreatitis as a model of visceral pain: A systematic mechanism-orientated approach

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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

Minor comments: 1. In the abstract and later in the paper, the authors state that increased intrapancreatic pressure within the parenchyma and/or pancreatic duct causing tissue ischemia (due to pancreatic duct strictures and stones) is one of the common mechanisms causing pancreatic pain. I have no problem to see the connection regarding the stones and the following complications. But we also have the duct strictures, originating either from tissue ischemia or can it be inflammation? Is the increased intrapancreatic pressure secondary to the initial changes (inflammation?) in the pancreatic tissue? If so, then the authors should accentuate this. In addition, this may also influence Table one, especially the order of mechanisms. 2. The authors state that they will focus on: QST, EEG and fMRI research concerning their application in chronic abdominal pain disorders such as chronic pancreatitis. In reality they focus on inflammatory visceral pain disorders i.e. CP and IBS representing a non-visceral i.e. altered visceral sensitivity phenomenon. 3. Regarding the EEG in chronic visceral pain: Resting state EEG. The authors state that in IBS patients, power spectrum analysis of the resting EEG showed a decrease of alpha power percentage together with an increase of beta power percentage compared to healthy subjects. They also report an increase in amplitude strength in the theta and alpha band in patients with CP compared to healthy controls and a significant shift toward lower frequencies in patients with CP compared with healthy controls. This was observed as a decrease in peak alpha frequency (PAF) over all scalp electrodes. I would suggest



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the authors to use a more united terminology or if not possible to try to clarify the different findings between the two states, if any. In my opinion this will shed light on the two different states. Furthermore, in the summary of this chapter the authors state that alpha activity in the resting state EEG has been shown to be affected in multiple chronic pain states. In other words they state that there is a change in the default state of the brain as a result of chronic pain. Do we really need an EEG to confirm that there is a change in the brain activity in pain disorders? In my opinion the authors should clarify how the future use of EEG (resting and evoked) could be used in a mechanism-orientated approach. 4. In the conclusion the authors state that QST may be helpful in diagnosing all the four questions in Table 2. Do this mean that QST can be used as a clinical tool to measure changes in the CNS accompanying chronic pain? Can the described actual QST setup be incorporated in the daily clinic, outside highly specialized units?