

July 22, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4176-review.doc).

Title: Pain and Chronic Pancreatitis: A Complex Interplay of Multiple Mechanisms

Authors: Jakob Lykke Poulsen, Søren Schou Olesen, Lasse Paludan Malver, Jens Brøndum Frøkjær & Asbjørn Mohr Drewes

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The manuscript has been improved according to the suggestions of reviewers:

- 1) Fax number has been added to the title page
- 2) Core tip has been added
- 3) Revision has been made according to the suggestions of the reviewers

Reviewer 00029378:

- a) A comment about clinical pain pattern and the correlation to the etiology of chronic pancreatitis has been inserted in the introduction.
- b) As there may be overlap, we have decided not to divide the different pain mechanisms in those probably involved in recurrent pain/pancreatitis with free intervals, and those probably involved in continuous pain, but agree that “wiring” problems are probably more involved in continuous pain, as described in the section about central sensitization.

Reviewer 00225271

- a) A description of lower thresholds to pressure pain in chronic pancreatitis patients with increased norepinephrine levels compared to patients with normal norepinephrine levels has been added to the section “ADDITIONAL CAUSES FOR PAIN”.
- b) Diabetic neuropathy and mesenteric ischemia are primarily considered as complications to and/or possible concomitant diseases that may contribute to the collective, abdominal pain in chronic pancreatitis patients, but a separate description of these causes are beyond the

scope of this review.

Reviewer 0070062

a) This review has no specific comments.

All revisions are highlighted in the revised document.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Med venlig hilsen/Best regards

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